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ESTIMATION OF PELVIC CAPACITY

Chairman's Address

WILLIAM F. MENGERT, M.D
Dallas, Texas

There are five components of cephalopelvic disproportion: (1) size and shape of the bony pelvis, (2) size of the fetal head, (3) force exerted by the uterus, (4) moldability of the head and (5) presentation and position. Of these, only the first is susceptible to accurate measurement. Attempts to measure the size of the unborn fetal head have not met with much success. Moreover, such distortion can occur during the birth process that, even if accurate prelabor cephalometry were possible, the problem of cephalopelvic relations could not be reduced to mathematic exactitude. In addition, there remain the three imponderables, force of labor, moldability of the fetal head and method of presentation, about which there is no possibility of acquisition of knowledge before the event of labor. In passing, it may be noted that as our group studies the progress of labor among women with contracted pelves, we are more and more impressed that the force of labor is one of the most important factors, if not the most important, influencing outcome. There were times, and patients with unbelievably small pelves, demonstrating again and again the principle that successful vaginal birth depends largely on the driving force. Therefore, the problem of cephalopelvic disproportion must remain in the realm of the art of medicine rather than of its science. Although this conclusion is inescapable, we should not therefore assume a defeatist attitude.

Modern knowledge concerning the obstetric capacity of the bony pelvis may be said to have originated in 1861 with Litzmann,[1] since he was the first to offer acceptable numerical criteria of size. It must be emphasized that his work, and that of his predecessor, Michaelis, was concentrated on the pelvic inlet. It remained for Williams[2] in 1909 to provide numerical criteria for the outlet. Acceptable midplane criteria are not yet available, largely because it was an unknown territory and also because of relative inaccessibility to other than radiographic measurement. Nevertheless, the subject of midplane capacity has its pioneer. In 1930, Hanson[3] of Stockton, Calif., devised an instrument for the manual measurement of the distance between the ischial spines and by 1936 reported a series of measurements in 3,941 women.[4] Despite this, and more recent publications, there are many who accord little significance to midplane contraction. Fascinating as the subject is, it is not the purpose of the present paper to concentrate attention on it. Rather, it is the purpose to consider evaluation of the obstetric capacity of the entire bony pelvis.

SUBJECTS

More than three years ago, the collection of information on cephalopelvic disproportion was begun at Parkland Hospital. At first, the pelves of selected patients, later those of all obstetric patients seen for the first time, were measured radiographically. Many difficulties, including the film shortage, intervened, so that to date our series numbers only 935 patients, of whom 592 have been delivered. The pelvis of each patient was measured manually and radiographically by obstetric-gynecologic residents, employing Snow's technic. The Department of Radiology of Parkland Hospital cooperated generously in making and processing the radiographs. The three planes were portrayed graphically[5] and a prediction of the outcome of labor made. Since early intervention could afford no useful information, patients were allowed to progress to second stage pains with the membranes ruptured. A few were delivered electively by the abdominal route, because of previous cesarean section or because the pelvis was so decidedly contracted that a trial of labor was absurd. The results, including infant birth weight and the outcome of labor, were tabulated on punch cards for ready analysis.

METHODS

When it is desired to transport a large piece of furniture through a small hallway, the obvious preliminary is measurement of the height and width of the narrowest doorways. In like fashion, measurement of the anteroposterior and transverse diameters of a sufficient number of cross sections of the bony pelvic canal will provide knowledge of its capacities. Since the bony pelvic canal is not long, the symphysis being about 4.5 and the sacrum 10 cm. from tip to promontory, three cross sections, inlet, midplane and outlet, will suffice for estimation of capacity. Figures 1, 2 and 3 show outlines of these planes of a normal gynecoid pelvis obtained, as described in a previous publication,[5] by shaping lead wire to the anatomic contours and correcting for minor variations. Except for

From the Departments of Obstetrics and Gynecology, Parkland Hospital and the Southwestern Medical College.

Read before the Section on Obstetrics and Gynecology at the Ninety-Seventh Annual Session of the American Medical Association, Chicago, June 24, 1948.

1. Litzmann, C. C. T.: Ueber den Einfluss der einzelnen Formen des engen Beckens auf die Geburt, Berlin, G. Reimer, 1861.

2. Williams, J. W.: Frequency, Etiology and Practical Significance of Contractions of the Pelvic Outlet, Surg., Gynec. & Obst. **8**: 619-638 (June) 1909.

3. Hanson, S.: A New Pelvimeter for the Measurement of the Bispinous Diameter, Am. J. Obst. & Gynec. **19**: 124-126 (Jan.) 1930.

4. Hanson, S.: Transversely Contracted Midpelvis with Particular Reference to Forceps Delivery, Am. J. Obst. & Gynec. **32**: 385-398 (Sept.) 1936.

5. Mengert, W. F., and Eller, W. C.: Graphic Portrayal of Relative Pelvic Size, Am. J. Obst. & Gynec. **52**: 1032-1040 (Dec.) 1946.

the outlet, the important diameters of each plane are the transverse and the anteroposterior. Since the outlet consists of two triangles with a common base and since the fetal head emerges through the posterior triangle, the posterior sagittal rather than the anteroposterior diameter of the outlet is employed. Six pelvic

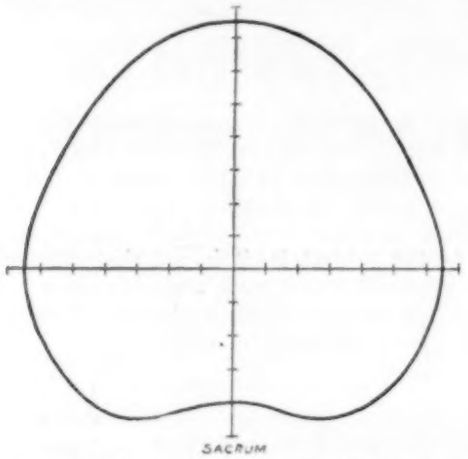

Fig. 1.—Normal inlet. (Reproduced from Mengert, W. F., and Eller, W. C.: Graphic Portrayal of Relative Pelvic Size, Am. J. Obst. & Gynec. 52: 1032-1040 [Dec.] 1946.) The anteroposterior measurement is 11.5, the transverse 13.0 and posterior sagittal 4.0.

measurements, the transverse and the anteroposterior of each plane, will therefore provide all practical information necessary for evaluation of pelvic capacity.

Obviously, this necessitates use of radiographic methods, since it is otherwise impossible to measure the transverse diameter of the inlet of the living woman. It is not intended to inaugurate, or encourage existing, discussion regarding the relative merits of manual or radiographic measurements. Manual measurements are accurate for those diameters possible to reach. Also, any of the commonly and currently employed radiographic technics is accurate beyond our needs. Weinberg and Scadron [6] measured the pelves of each of 100 patients within 0.1 cm. by four radiographic methods. The radiographic method currently employed

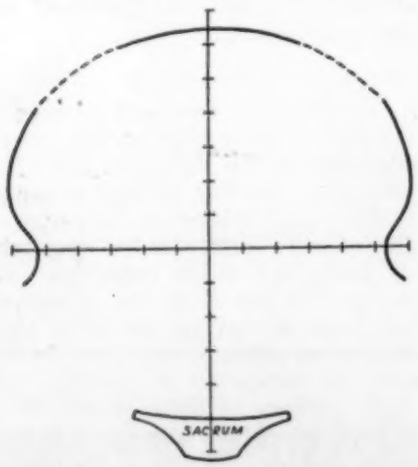

Fig. 2.—Normal midplane. (Reproduced from Mengert, W. F., and Eller, W. C.: Graphic Portrayal of Relative Pelvic Size, Am. J. Obst. & Gynec. 52: 1032-1040 [Dec.] 1946.) The anteroposterior measurement is 11.5, the transverse 10.5 and the posterior sagittal 5.0.

at Parkland Hospital was validated in two ways: by direct measurement with calipers and ruler during the course of gynecologic operations and through check of the same patient by different observers. No error of more than 5 mm. was found. This is believed to represent a degree of accuracy exceeding the requirements of the situation.

In summary, it may be reiterated that method of measurement is unimportant. The interpretation and evaluation of pelvic capacity, after the measurements are obtained by whatever method, are the problems confronting the obstetrician. They can be solved only in conjunction with the experience gained through years in the delivery room. The opinion of a man who has not repeatedly followed the course of labor and does not know the extent of the forces concerned is valueless and worse; it is confusing.

INTERPRETATION

Many methods of evaluation of pelvic capacity were tried. At first, they consisted of fitting an outline cross section of the fetal head to the graphs of the various pelvic planes. Next, the sum of the posterior sagittal and transverse diameters was utilized as an index both for the outlet and midplane, with fair success. Nevertheless, some glaring discrepancies were observed. For example, a patient with the lower portion of the sacrum decidedly bent forward, and therefore with a very short posterior sagittal of the midplane, experienced an easy spontaneous labor. Review of the situation showed ample room anterior to the ischial spines. Moreover, this method was totally unsatisfactory for the inlet. The next logical step in the attempt to evaluate capacity was the utilization of the sum of the transverse and the entire anteroposterior diameter of the inlet or midplane. This gave more consistent results than other methods and led directly to the final and best method, calculation of the area of these two planes. At first, areas were measured with a planimeter, carefully tracing the outlines and accurately recording the precise value in square centimeters. However, the actual figures are immaterial, since the relation of one pelvis to another, or of one plane to another, is the important consideration. Finally, the simple expedient of multiplying the transverse and the anteroposterior diameters and expressing the capacity of the various planes in terms of the product of these diameters was employed. Comparison of the two methods indicated no significant difference between them. The product of the two diameters of each plane is as satisfactory a measure of relative capacity as the more laboriously obtained measurement of the actual area. A norm can be established for each plane and its capacity expressed in percentage of normal. Thus, it is possible to compare not only one pelvis with another, but also two planes of the same patient. For example, a patient with an inlet capacity of 75 per cent of normal

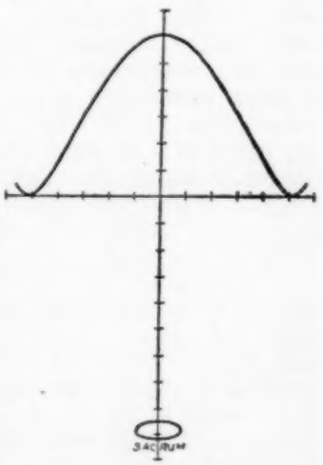

Fig. 3.—Normal outlet. (Reproduced from Mengert, W. F., and Eller, W. C.: Graphic Portrayal of Relative Pelvic Size, Am. J. Obst. & Gynec. 52: 1032-1040 [Dec.] 1946.) The transverse measurement is 10.0 and the posterior sagittal 8.5.

6. Weinberg, A., and Scadron, S. J.: Value and Limitations of Pelvioradiography in Management of Dystocia, with Special Reference to Midpelvic Capacity, Am. J. Obst. & Gynec. 52: 255-263 (Aug.) 1946.

and a midplane capacity of 90 per cent is far better off obstetrically than a patient with the reverse conditions.

RESULTS

Average and Distribution of Measurements.—The essential pelvic measurements (table) include the transverse and the anteroposterior of the inlet and midplane and the transverse and posterior sagittal of the outlet. The transverse is accorded priority, since engagement generally occurs in this diameter of the inlet and internal rotation is hindered by a narrow midplane.

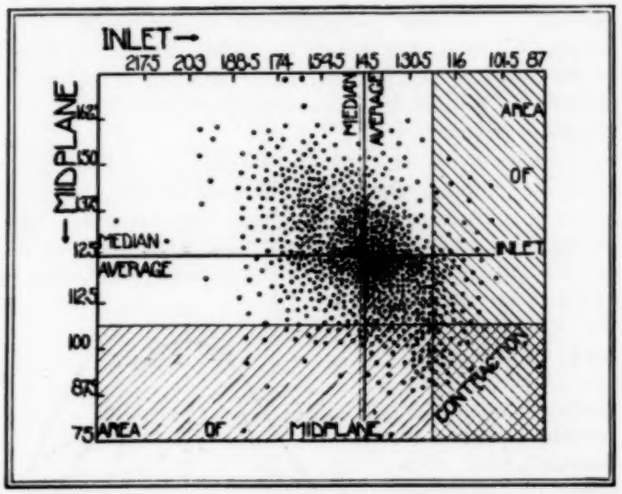

Fig. 4.—Distribution of 935 inlet and midplane capacities, expressed as areas (square centimeters). Roughly, the arrangement is linear from large to small. In other words, the inlet and midplane tend to vary together. Association of a large inlet with a small midplane, or the reverse, tends to be uncommon. The shaded area represents patients whose inlet or midplane capacities were 85 per cent, or less, of normal.

Moreover, with an adequate transverse diameter in any plane, there is seldom dystocia at that level.

The average values of the diameters as measured in 935 patients conform closely to accepted standards published by Stander.[7] After the inlet and midplane

Essential Pelvic Measurements

	Accepted Standards	Average 935	Product, Ap. × Trans.
Inlet			
Transverse	13.0	12.5	145.0
Anteroposterior	11.5	11.6	
Midplane			
Transverse	10.5	10.3	124.9
Anteroposterior	11.5	12.1	
Posterior sagittal	5.0	4.5	
Outlet			
Transverse	10.0	10.6	
Posterior sagittal	8.5	8.8	

* There are six essential pelvic measurements, including the transverse and anteroposterior of each plane. The posterior sagittal of the midplane is included merely for interest.

products were obtained, the central tendency of each was calculated. For the inlet it was: average 145, median 146 and mode 143. For the midplane it was: average 124.9, median 126 and mode 121. The average values, rather than the median or mode, were utilized and 145 accepted as normal for the inlet and 125 as normal for the midplane. These figures represent 100 per cent, for each plane, respectively, and capacity is expressed in percentage in relation to them.

7. Stander, H. J.: Textbook of Obstetrics, New York, D. Appleton-Century Company Inc., 1945.

The entire series is illustrated graphically as a scatter diagram in figure 4. Broadly, the arrangement is linear, from large to small, indicating that inlet and midplane tend to vary together. In other words, association of a large inlet with a small midplane, or the reverse, is relatively uncommon. There are, of course, glaring exceptions to this rule.

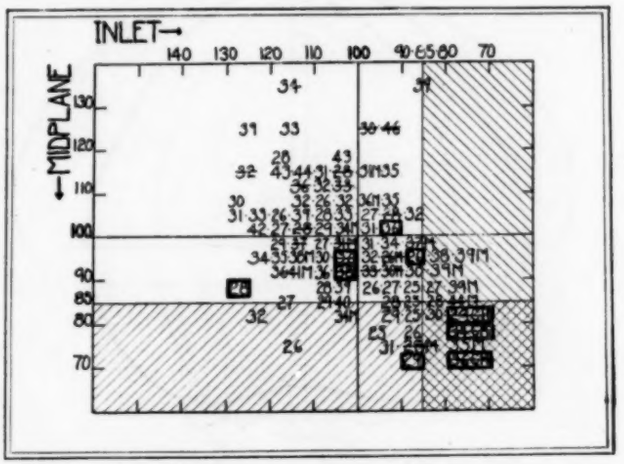

Fig. 5.—Vaginal operations of necessity in 97 cases (inlet and midplane capacities) expressed as percentage of average. The midplane forceps operations tended to concentrate in the areas of less than average capacity, and all three craniotomies were performed in women with both inlet and midplane contractions. The numbers represent weight of infants in hundreds of grams; a horizontal line through a number represents labor more than thirty hours; M is midplane forceps operation; a square enclosing a number represents fetal death, and CR is craniotomy.

By a process of trial and error, it became obvious that 85 per cent of normal capacity of either inlet or midplane represented the border line between adequacy and contraction. The area of 85 per cent or less capacity is shaded in figure 4 and subsequent figures.

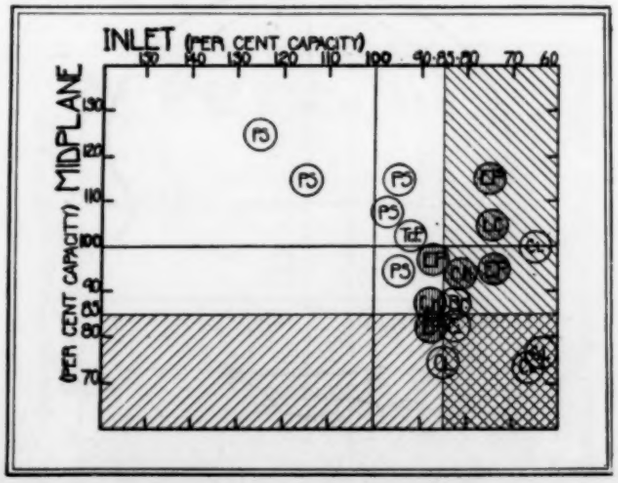

Fig. 6.—Graphic representation of data of cesarean section in 19 cases. Trial of labor, terminated by low cervical, extraperitoneal or cesarean hysterectomy, was permitted in patients with borderline pelves. In most instances the trial was allowed to progress to second stage labor with the membranes ruptured. Elective abdominal delivery (without antecedent labor) was performed either in those women with indications other than cephalopelvic disproportion or in those with such frank contraction that a trial of labor was absurd. Plain circles represent cesarean section before onset of labor; circles with vertical hatching represent section after onset of labor; PS is previous section, CL classic section, LC low cervical section, EP extraperitoneal section and CH cesarean hysterectomy.

So far, little has been said concerning the outlet. It is doubtful whether outlet contraction exists as a sepa-

rate entity, unassociated with midplane contraction. This was evidenced in the present series by the fact that the intertuberous diameter between the ischial bones was shorter than the interspinous in only two instances, and then the difference was negligible. In other words, the transverse diameter of the midplane is

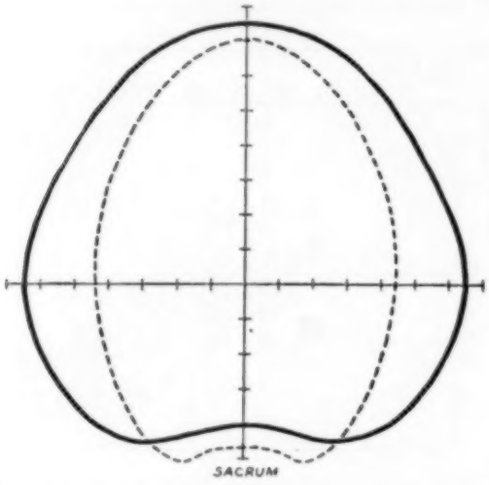

Fig. 7.—Pelvis of M.P. (reproduced from Mengert, W. M., and Eller, W. C.: Graphic Portrayal of Relative Pelvic Size, Am. J. Obst. & Gynec. **52**: 1032-1040 [Dec.] 1946.) Although the inlet would appear to be barely adequate, its capacity is only 69 per cent of average.

commonly shorter than the transverse diameter of the outlet. There is no congenital anomaly or acquired disease which will narrow the tuberosities of the ischium without also narrowing the lower part of the innominate bones. In other words, there can be no serious outlet contraction without commensurate contraction of the midplane. Finally, much of what, in the past, we have termed outlet contraction actually is midplane contraction. When the vertex of the fetal

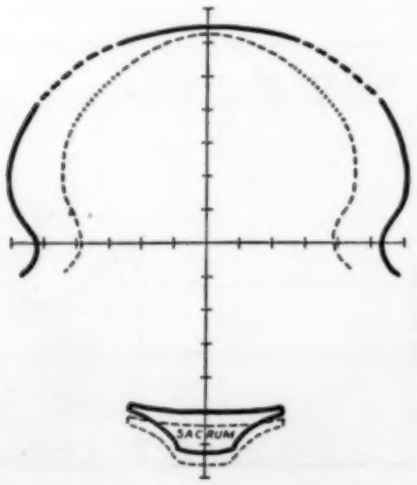

Fig. 8.—Midplane of patient of figure 7. (Reproduced from Am. J. Obst. & Gynec. **52**: 1032-1040 [Dec.] 1946.) Capacity is 72 per cent of average.

head has traversed a contracted midplane and is visible between the parted labia, the biparietal diameter is at least 7 cm. higher in the birth canal. This has been repeatedly demonstrated during the past few months by checking the progress of obstructed labors with lateral roentgenograms. They showed clearly that obstruction, when the vertex was on the perineum, was not at the ischial tuberosities, but at the level of the midplane, or above. This will be the subject of a forthcoming presentation by one of the members of the department.

Operations of Necessity.—Figure 5 shows the distribution and outcome of vaginal operations of necessity among the 592 delivered women. There were seventy-three low forceps operations, twenty-one midplane forceps operations and three craniotomies. Low forceps operations of necessity were defined, for the purposes of this paper, as those performed after a two hour second stage arrest of labor. There was no time limit for midplane forceps operations. The majority of the low forceps operations occurred in patients anesthetized by means of caudal or spinal block. The midplane forceps operations tended to be concentrated in the areas of pelvic contraction, and all three craniotomies took place in women with combined inlet and midplane contractions.

Cesarean Sections.—Nineteen cesarean sections were performed among the 592 delivered women, an incidence of 3.2 per cent, or 1 in 31. This relatively high incidence of abdominal delivery was occasioned by the fact that the pelves of most of the patients submitted to cesarean section were measured radiographically, automatically including them in the present series. In contrast, the incidence of cesarean section for the entire service during the same period of time was 0.55 per cent, or 1:181, representing twenty-three sections among 4,183 patients. Figure 6 shows the distribution of the nineteen cesarean sections among the subjects of this paper. These were performed on 18 women, two sections being done on the patient with the smallest pelvis in the series. It will be noted that elective abdominal delivery, without antecedent labor, was performed either in those women with indications other than cephalopelvic disproportion, or in those with obviously severe contraction. Moreover, since the trials of labor were continued into the second stage, and thus were not gestures, either extraperitoneal section or cesarean hysterectomy became the operation of choice on conclusion of the trial.

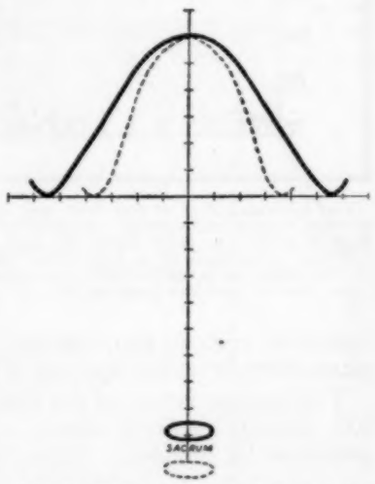

Fig. 9.—Outlet of patient of figure 7 (reproduced from Mengert, W. F., and Eller, W. C.: Graphic Portrayal of Relative Pelvic Size, Am. J. Obst. & Gynec. **52**: 1032-1040 [Dec.] 1946).

The pelvis of the patient M. J., with the most pronounced contraction in the series, has been portrayed graphically elsewhere.[5] It is worth reproducing (figs. 7, 8 and 9) here for several reasons. Morphologically the pelvis is anthropoid in type and illustrates the principle that transverse narrowing is serious. For example, although the inlet would appear to permit passage of an average head, it had but 69 per cent of capacity. The midplane appeared to be less fit to permit passage of the fetal head, but its capacity actually was 72 per cent of average. This patient submitted to elective cesarean section in two successive pregnancies. This case is in contrast with that of H. L. J.

(figs. 10 and 11). The inlet appears to be small, but had 82.5 per cent of average capacity. There was only 73 per cent of average midplane capacity, but sufficient room anterior to the spines to permit passage of the head in a transverse position. The first stage of labor lasted 23 hours, the second one hour, and a living child weighing 2,912 Gm. was born spontaneously. These 2 patients illustrate quite well the comparison of pelves and planes when capacity is expressed in terms of per cent of average.

Mortality.—There was no maternal death in the series. There were 26 fetal deaths, of which 12 were due to causes including anomaly, prematurity, syphilis and accidents of pregnancy. There were 14 fetal deaths related to cephalopelvic disproportion or which were unexplained (fig. 12). Causes included tentorial tear and scalp injury with hemorrhage and craniotomy. There was a tendency for fetal deaths to be concentrated in, and toward, the areas of less than average pelvic capacity.

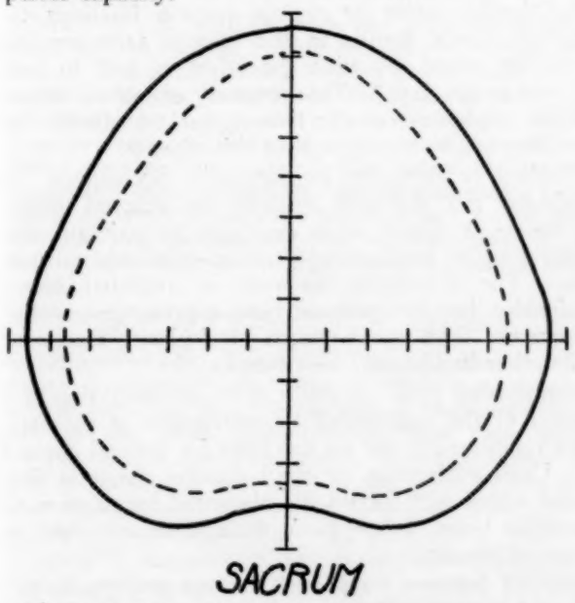

Fig. 10.—Although this inlet looks small, its capacity is 82.5 per cent of average.

COMMENT

Radiographic pelvic measurement is not feasible for all pregnant women. Moreover, it is unnecessary when manual methods indicate an obviously adequate pelvis. Therefore, an attempt was made in a previous publication [8] to enumerate criteria of suspicion indicating the necessity for employment of radiographic methods. They should be employed in the presence of any one of the following observations:

A. History
1. Difficult labor, especially midforceps delivery
2. Unexplained stillbirth

B. Palpation
1. Prominent ischial spines
2. Sacral deformity (any, but especially forward angulation)

C. Manuel mensuration
1. Inlet
   (*a*) Ability to touch sacral promontory on vaginal examination.
   (*b*) External measurements below average; i. e., interspinous 23 cm. or less, intercristal 26 cm. or less and external conjugate 17 cm. or less
2. Outlet
   (*a*) Bisischial 8.5 cm. or less
   (*b*) Sum of bisischial and posterior sagittal 15.0 cm. or less

D. Nonengagement of fetal head at term in a primigravida

8. Eller, W. C., and Mengert, W. F.: Recognition of Midpelvic Contraction, Am. J. Obst. & Gynec. **53**: 252-258 (Feb.) 1947.

There are some who will insist that harm, as a direct result of failure to perform cesarean section, must inevitably accrue to some women. There can be no disagreement with this view. There were two vesicovaginal fistulas resulting, respectively, from craniotomy and a serious midplane forceps operation. Less

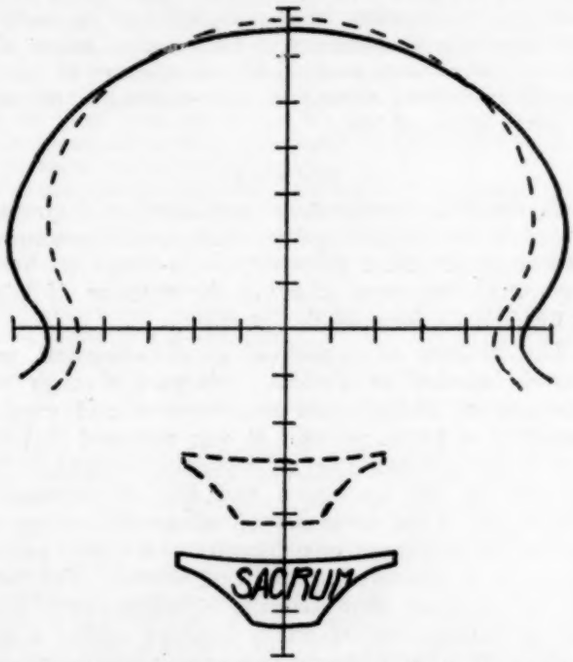

Fig. 11.—Midplane of patient of figure 10. Although the capacity is 73 per cent of average, there is sufficient room anterior to the spines. After twenty-four hours of labor, the patient was delivered spontaneously of a 2,912 Gm. living child.

obvious, but commoner, was puerperal pelvic cellulitis or, as observed clinically, prolonged morbidity. When the pelvic cellular tissues are compressed and squeezed between the fetal head and the maternal bones, and thus rendered partially or totally ischemic for protracted periods of time, they may be readily victimized by invading bacteria. Following difficult labor, there is generally endometritis. Although of short duration

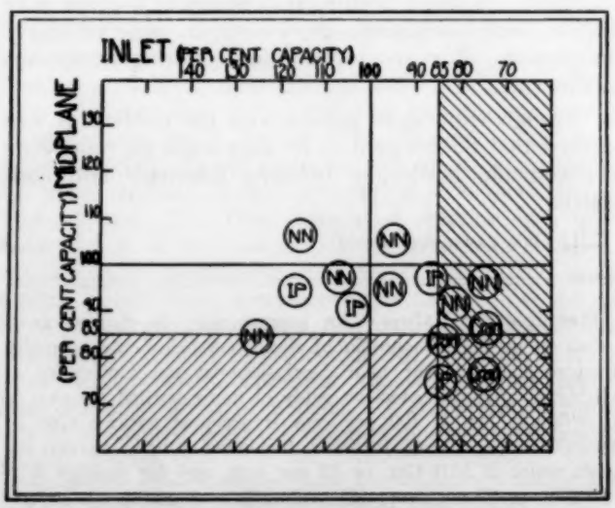

Fig. 12.—Fourteen fetal deaths related to disproportion or which were unexplained. All fetal deaths in term-sized infants, known to be alive at the onset of labor, whose mothers were free of diseases such as syphilis and eclampsia, are included here. Note the tendency to concentrate in and toward the areas of less than average pelvic capacity. (*NN* is neonatal; *IP* is intrapartum; *Cran* is craniotomy.)

and disappearing spontaneously, the endometritis institutes infection in the devitalized parauterine and paravaginal cellular tissues because of lowered resistance.

On the other hand, it was amazing how many seemingly impossible cephalopelvic disproportions disappeared under the driving force of the uterus. The resulting spontaneous labor was followed by normal and speedy convalescence. Conversely, when the uterine forces were poor, pelvic contraction of minor degree sometimes offered an insurmountable obstacle to the progress of labor.

SUMMARY

Of the five components of cephalopelvic disproportion, only one, the bony pelvis, is susceptible to accurate measurement. Next to pelvic size, perhaps the most important component affecting the outcome of labor is the driving force of the uterus.

The subject of cephalopelvic disproportion was actively studied at Parkland Hospital through the mediums of radiographic measurement and graphic portrayal of pelvic planes. It was observed that the best index of either inlet or midplane capacity is the product of the transverse and the anteroposterior diameters. This necessitates radiographic measurement, since the transverse diameter of the inlet cannot otherwise be measured in the living woman. The manner of obtaining measurements is unimportant, since any acceptable method offers accuracy within a few millimeters. The problems confronting the obstetrician are, therefore, interpretation of measurements and evaluation of capacity, not the making of measurements.

After determination of the index of average inlet or midplane capacity by multiplication of the transverse and the anteroposterior diameters, a given pelvis could be compared with the average in terms of percentage.

In general, inlet and midplane tended to vary together. In other words, association of a large inlet and a small midplane, or vice versa, was relatively uncommon. There were, of course, glaring exceptions to this rule.

Through experience gained with the method, it was learned that 85 per cent of average capacity represents a reasonable borderline between adequacy and contraction.

2211 Oak Lawn Avenue (4).

Hemoglobin Values.—An anemia may be defined as a reduction in the hemoglobin of the blood below the normally accepted values. Our own conclusions at the University of Michigan, after an extensive study of many normal persons, is as follows: (1) If 100 per cent is accepted as 15.6 Gm. of hemoglobin per 100 cc. of blood, the lower limit of normal for adult males is 13.0 Gm. or 83 per cent, and for females it is 12.0 Gm. or 77 per cent; (2) ordinarily patients do not experience the usual symptoms of an anemia unless the hemoglobin falls to the vicinity of about 11 Gm. or 70 per cent, or lower; (3) the physiologic anemia of pregnancy, due entirely to dilution of the circulating blood, may lower the hemoglobin of a pregnant woman to 64 per cent under normal conditions. Hence a true anemia of pregnancy is not present unless the hemoglobin is below this figure.—Sturgis, Cyrus C., M.D., *Official Journal of the Interstate Postgraduate Medical Association—Postgraduate Medicine*, June 1948.

STUDIES OF HEMOPHILIA

I. The Control of Hemophilia by Repeated Infusions of Normal Human Plasma

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and
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Boston

No method of therapy has hitherto been devised which has proved effective in the long-continued control of hemophilia. The purpose of this paper is to report the effects of repeated infusions of normal plasma on the delayed blood coagulation and on the hemorrhagic tendency of this disease. Our observations on patients treated over a period of ten to twenty months indicate that this therapeutic approach provides a basis for amelioration of the bleeding tendency with significant rehabilitation of such patients.

Most observers [1] have agreed that the addition of whole blood, plasma or certain plasma fractions to hemophilic blood results in the prompt reduction of the clotting time. In vivo the effect is said to last from two to six days.[2] This property of normal blood probably explains the effectiveness of transfusion in controlling acute hemorrhage in this disease.

Whether or not the hemorrhagic phenomena in hemophilia are referable entirely to delayed blood coagulation, it would seem desirable to maintain the clotting time of hemophilic blood at relatively normal levels. The difficulties inherent in repeated blood transfusions for this purpose over a prolonged period are obvious. The use of plasma or of plasma fractions, on the other hand, is far less difficult.

Despite some progress made in the concentration and isolation of the antihemophilic component of plasma,[3] potent fractions are not yet available for general clinical use. Until such time, or until another agent is discovered which will correct the abnormal coagulation of hemophilic blood, prophylactic therapy must consist of the use of plasma.

In 1942 Johnson [4] reported the successful management of 1 patient with hemophilia by means of lyophile human plasma administered weekly for three months, a period which is inadequate to evaluate any therapy accurately in view of frequent remissions and exacerbations of the hemorrhagic phenomena in this disease.

From the Medical Research Laboratories, Beth Israel Hospital, and the Department of Medicine, Harvard Medical School.

1. (*a*) Weil, P. E.: Étude du sang chez les hémophilies, Bull. et mém. Soc. méd. d. hôp. d. Paris **23:** 1001, 1906. (*b*) Sahli, H.: Weitere Beiträge zur Lehre von der Hämophilie, Deutsches Arch. f. klin. Med. **99:** 518, 1910. (*c*) Fonio, A.: Die Hämophilie, Ergebn. d. inn. Med. u. Kinderh. **51:** 443, 1936. (*d*) Patek, A. J., Jr., and Stetson, R. P.: Hemophilia: I. The Abnormal Coagulation of the Blood and Its Relation to the Blood Platelets, J. Clin. Investigation **15:** 531, 1936. (*e*) Patek, A. J., Jr., and Taylor, F. H. L.: Hemophilia: II. Some Properties of a Substance Obtained from Normal Human Plasma Effective in Accelerating the Coagulation of Hemophilic Blood, J. Clin. Investigation **16:** 113, 1937. (*f*) Lozner, E. L., and Taylor, F. H. L.: The Coagulation Defect in Hemophilia: Studies of the Clot Promoting Activity Associated with Plasma Euglobulin in Hemophilia, J. Clin. Investigation **18:** 821, 1939. (*g*) Minot, G. R.; Davidson, C. S.; Lewis, J. H.; Tagnon, H. J., and Taylor, F. H. L.: The Coagulation Defect in Hemophilia: The Effect in Hemophilia of the Parenteral Administration of a Fraction of the Plasma Globulins Rich in Fibrinogen, J. Clin. Investigation **24:** 704, 1945.

2. Jones, H. W., and Tocantins, L. M.: The Treatment of Hemophilia, J. A. M. A. **103:** 1671 (Dec. 1) 1934.

3. Patek and Taylor.[1e] Bendien, W. M., and von Creveld, S.: Investigations on Hemophilia: II., Maandschr. v. kindergeneesk. **6:** 186, 1937. Taylor, F. H. L.; Davidson, C. S.; Tagnon, H. J.; Adams, M. A.; MacDonald, A. H., and Minot, G. R.: Studies in Blood Coagulation: The Coagulation Properties of Certain Globulin Fractions of Normal Human Plasma in Vitro, J. Clin. Investigation **24:** 698, 1945.

4. Johnson, J. B.: Management of Hemophilia with Lyophile Human Plasma Intravenously Injected, J. A. M. A. **118:** 799 (March 7) 1942.

Furthermore, Munroe and Jones[5] described a patient whose disease, after many blood and plasma transfusions, became increasingly refractory to their effects. Refractoriness also to the antihemophilic property of certain plasma fractions has been described.[6] Since the beneficial clot-promoting effects of blood or plasma would appear promising in the prophylactic management of hemophilia, it is of the utmost importance to determine whether such refractoriness commonly develops consequent to their frequent use over a long interval.

In view of the evanescent effect of any single plasma infusion it must be given more often than once a week in order to maintain a reduced clotting time. For this reason, our patients were given plasma three to four times weekly for ten to twenty months. Laboratory and clinical observations made during this time are here presented.

PROCEDURE

Four subjects were treated:

CASE 1.—T. K., aged 24 years, had group B, Rh-negative blood, with an original clotting time of sixty-five to ninety minutes. One of his mother's brothers died of severe bleeding, and one of his own brothers who died at the age of 6 months was thought to be a bleeder. From the age of 1½ years there were numerous hemorrhages into joints, muscles, genitourinary tract and from gums. The patient was frequently incapacitated, with innumerable hospital admissions. He was studied for years at another hospital, where weekly plasma therapy for two years was ineffective in preventing hemorrhages. He was never employed steadily because of frequent hemorrhages.

During the present study the patient received two hundred and six infusions of 150 cc. of plasma three times weekly for eighteen months. For another one and one-half months, because of a hemorrhagic episode described later, the patient received 100 to 150 cc. of plasma daily or twice daily. Thereafter he was given plasma therapy three times weekly. Throughout the observation period of twenty months there were several lapses in therapy of four days to one month when the patient left town on holidays. Total plasma injected was approximately 38 liters.

CASE 2.—I. G., aged 28, had group O, Rh-positive blood, with an original clotting time of one hundred and twenty minutes. One brother died in infancy of hemorrhage. The patient had experienced bleeding episodes since the age of 6 into joints and muscles, from mucous membrane and into the genitourinary tract. He was severely crippled and incapacitated, and had been studied and treated for years at another hospital.

He received two hundred and seventy infusions over nineteen months, totaling approximately 41 liters, as follows: 150 cc. three times weekly for nine months; four times weekly for one and one-half months; daily for one and one-half months; four times weekly for five and one-half months, and three times weekly thereafter.

There were occasional short lapses (four to five days) for experimental purposes and one (ten days) because of illness (episode of jaundice) preventing his return to laboratory for scheduled treatment.

CASE 3.—R. R., aged 17 years, had group A, Rh-positive blood, with an original clotting time of one hundred and eighty minutes. There was a negative family history. The patient had had hemorrhages since early infancy, into joints mostly, and from deciduous teeth. He was hospitalized ninety times and was considerably crippled, unable to attend school.

This patient received one hundred and seventy-three infusions of 180 cc. three times weekly for thirteen months, totaling about 31 liters. There was one four day lapse, when icy road conditions prevented the patient from coming to the hospital for scheduled treatment.

CASE 4.—C. R., aged 8 years, had group O, Rh-positive blood. The family history was positive for hemophilia. The patient had had hemorrhages since early childhood into joints and muscles, interfering seriously with school work. His physical activity was restricted. He was first seen by us because of severe hemorrhage into the gastrocnemius muscle.

He received one hundred and eleven infusions of plasma, 100 cc. three times weekly for ten months. There was one lapse of two and one-half weeks when the patient was confined to his home because of chickenpox.

The plasmas were prepared as follows: 250 cc. "pyrex" glass centrifuge bottles containing 25 cc. of 2.5 per cent sodium citrate solution were filled with blood from normal subjects,[7] capped and centrifuged[8] for fifteen to twenty minutes at 2,000 revolutions per minute.

The supernatant plasma was removed with a syringe and placed, in amounts of 100, 150 or 180 cc., into a dry Fenwal flask. The bottled plasma was then quickly frozen and stored in the frozen state[9] at 10 F. Sterile technic was used throughout. Bloods with positive serologic tests for syphilis were excluded.

Some flasks contained plasma of two to three blood groups; most, however, contained plasma of only one type. No attempt was made to give plasma of homologous type, although for the first six months all donors were typed. Since no reactions could be attributed to incompatibility, typing was discontinued thereafter.

Immediately prior to administration the frozen plasma was thawed in a water bath at body temperature or less, filtered quickly through a stainless steel 150 mesh filter into another Fenwal flask, and administered intravenously in five to ten minutes with a Fenwal set.

Determinations of the coagulation time, by a modification of the Lee and White method,[6a] were frequently made immediately before, immediately after and twenty-four, forty-eight and seventy-two hours after administration of plasma.

Occasionally, plasma was withheld in order to permit observation on the height to which the clotting time would rise and to reevaluate quantitatively the clot promoting effect of plasma in vivo and in vitro.[10]

LABORATORY OBSERVATIONS

The infusion of plasma was always followed, almost immediately, by a pronounced drop in the coagulation time to normal or near normal limits.[11] The clotting time remained low during the first twenty-four hours, increased gradually during the subsequent day and, unless another plasma injection was given, returned to its previous level within seventy-two or more hours (figs. 1 and 2). This pattern of reaction was uniform for 3 of the subjects who were thus studied. Variations in coagulation time were seen in the same patient twenty-four, forty-eight and seventy-two hours after any single plasma infusion, and a difference was noted from patient to patient in the average clotting time twenty-four, forty-eight or seventy-two hours after administration of plasma. The difference could not be correlated with the original clotting time before plasma therapy.

5. Munroe, F. L., and Jones, H. W.: The Detrimental Effect of Frequent Transfusions in the Treatment of a Patient with Hemophilia, Am. J. M. Sc. **206**: 710, 1943.

6. (*a*) Pohle, F. J., and Taylor, F. H. L.: The Coagulation Defect in Hemophilia: The Effect in Hemophilia of Intramuscular Administration of a Globulin Substance Derived from Normal Human Plasma, J. Clin. Investigation **16**: 741, 1937; (*b*) The Coagulation Defect in Hemophilia: Studies on Refractory Phase Following Repeated Injections of Globulin Substance Derived from Normal Human Plasma in Hemophilia, ibid. **17**: 779, 1938.

7. Dr. Mark Lesses, Director of the Blood Bank, Harriet Sheffreen, in charge of the Volunteer Blood Donors, and volunteer blood donors cooperated in making blood available for this purpose.

8. Since the antihemophilic principle of plasma is labile, particularly in whole blood,[9] most of the blood was processed within one-half hour after withdrawal.

9. Under such conditions, antihemophilic potency remains unaffected for at least five months.

10. Alexander, B., and Landwehr, G.: Studies on Hemophilia: II. Assay of the Anti-Hemophilic Clot Promoting Principle in Normal Human Plasma with Some Observations on the Relative Potency of Certain Plasma Fractions J. Clin. Invest. **27**: 98, 1948.

11. The normal range for the clotting time was considered to be 4-11 minutes.

In none of the patients did the disease become refractory to the effects of normal plasma. There was, furthermore, no evidence that by maintaining the coagulation time at levels more closely approximating normal, the underlying defect in blood coagulation was

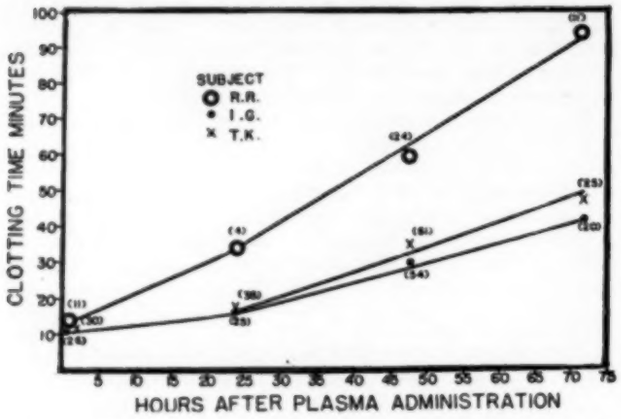

Fig. 1.—Effect of repeated infusions of normal human plasma on clotting time of hemophilic blood. The numeral in parentheses represents the number of determinations of the clotting time at the designated interval. The points on the curves represent the averages of these determinations.

any less at the end than at the beginning of the therapeutic regimen described.

The over-all effect of repeated infusions of plasma is indicated diagramatically in figure 3. Despite peaks in clotting time reached immediately before each administration of plasma, the average clotting time was greatly reduced.

As little as 1 cc. of intravenously administered normal plasma hastens the coagulation of hemophilic blood. The duration of this effect varies with the dose (fig. 2; table 1). Ten cubic centimeters may lower the clotting time to relatively normal limits, but the effect lasts for a shorter interval than when 100 or 150 cc. are used.

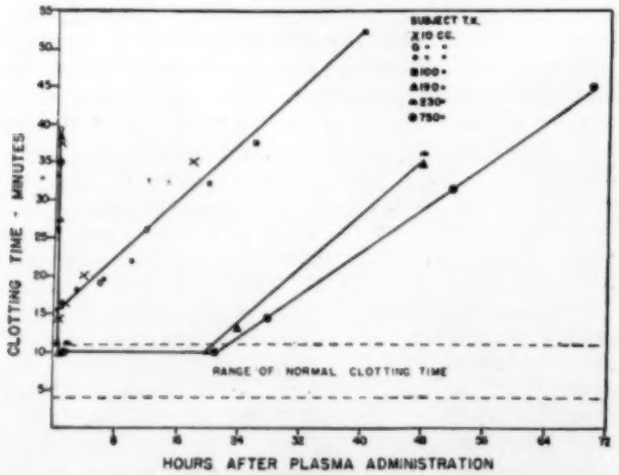

Fig. 2.—The effect of varying amounts of normal plasma administered intravenously on the coagulation time of hemophilic blood.

Larger amounts produce a more sustained action, but the prolongation of the effect is not directly proportional to the dose. The effects of 50 or 100 cc. of plasma are at times practically indistinguishable from the effects of 10 cc., and the difference between 750 and 230 cc. is slight.

Intramuscularly administered plasma appears to be far less effective in hastening the coagulation of hemophilic blood (table 2). As much as 30 cc., 15 cc. injected into each buttock followed by five minute massage of the injection site, failed to reduce the clotting time as much as 1 cc. given intravenously. The slight effect which was obtained appeared in one-half to one hour after injection, whereas intravenous plasma acts almost immediately.

It is noteworthy that plasma, even in amounts of 650 to 750 cc., does not reduce the clotting time much below the upper limit of normal. Most often it ranged, immediately after infusion, between eleven and fifteen minutes (fig. 3).

CLINICAL OBSERVATIONS

Case 1.—The clinical course of all the patients during this period of prolonged prophylactic therapy was strikingly improved. Patient 1 was free of major

TABLE 1.—*Effect of Infusions of Varying Amounts of Normal Plasma on Coagulation Time of Hemophilic Blood*

	Amount		Clotting Time (Minutes) Time After Injection					
				Hours				
Subject	Injected, Cc.	Before Injection	Min. 10	6	10	24	48	
RR	2.0	116	58	..	..	..	..	
	10.0	112	23	30	30	57	..	
	50.0	57	17	..	..	39	68	
	100.0	106	11	..	..	..	47	
	150.0	110	11	..	..	26	50	
	180.0*	90±	11	..	..	33	58	
TK	1.0	121	44	..	..	..	..	
	10.0	40	16	18	24	37	..	
	100.0	26	11	..	..	36	52†	
	150.0*	40	11	..	..	18	35	
	190.0	39	10	..	..	13	35	
	230.0	28	12‡	..	..	11§	35	
	750.0	35	11¶	..	..	10‖	22#	
	.....	..	..	..	..	15**	32††	
IG	10.0	32	17‡‡	21	30	42§§	..	
JG	1.0	120	59	..	..	..	..	
	1.5	150	51	..	..	..	..	
	3.0	160	34	..	..	..	..	
	150.0	160	12	..	..	..	55	
	650.0	186	10	..	14¶¶	27‖	50	63‖‖ 140##

* Average of many observations (fig. 1).
† Forty hours after injection.
‡ One and three-fourths hours after injection.
§ Twenty hours after injection.
¶ One and one-half hours after injection.
‖ Twenty-one hours after injection.
Forty-four hours after injection.
** Twenty-four hours after injection.
†† Fifty-two hours after injection.
‡‡ Three-fourths hour after injection.
§§ Twenty-six hours after injection.
¶¶ Thirteen hours after injection.
‖‖ Sixty-six hours after injection.
Eighty-seven hours after injection.

hemorrhagic episodes throughout the time that he received plasma regularly despite greatly increased activity (swimming, bowling, baseball, basketball, gymnastics, squash, running, horseback riding). In no instance was there more than localized ecchymosis even following types of trauma which had hitherto resulted in moderate to severe hemorrhage. Hemostasis in dental care involving scraping the gums was greatly simplified. For the first time, the patient was able to do sustained remunerative work for one and one-half years.

This patient experienced four significant hemorrhagic episodes. The first occurred five days after a plasma infusion, when, while on a short holiday (five days) the patient fell down some steps, incurring severe trauma to arm and leg. The second hemorrhage, hematuria, developed after four days without plasma, again while the patient was traveling. This subsided within one week after plasma therapy was resumed.

A third episode, oozing from an extensive pyogenic ulceration of the buccal mucosa, which persisted despite plasma therapy, ceased dramatically after the first of several penicillin injections administered in doses of 200,000 units with each plasma infusion for one week. The ulcer cleared promptly. The fourth episode occurred spontaneously when the subject was again on a month's holiday; incapacitating hemarthroses developed five days after the last plasma and were followed later by hematuria. Hematuria persisted for six weeks despite several whole blood transfusions and infusion of plasma daily or twice daily, each of which reduced the coagulation time to normal range. The addition of penicillin to some of the plasmas was also ineffective in instituting hemostasis.

TABLE 2.—*Comparative Effect of Intravenously and Intramuscularly Administered Normal Plasma on Coagulation Time of Hemophilic Blood* *

Route of Administration	Plasma Injected, Cc.	Clotting Time (Minutes) Before Injection	Minutes After Injection 8-11	30	60	180	240
Intravenous.....	1.0	120	50	..	..	..	..
	1.5	150	51	..	..	..	..
	3.0	160	34	..	..	..	..
Intramuscular...	2.0	160	160	..	..	..	..
	10.0†	150	150	140	..	..	..
	30.0‡	169	..	140	..	..	..
	30.0‡	144	..	..	75	85	68

* Each experiment was done on a different day. Normal plasma used in each experiment was demonstrated to be fully potent by simultaneous in vitro assay.[10]
† Five cubic centimeters into each triceps.
‡ Fifteen cubic centimeters into each buttock.

Case 2.—The second subject had suffered extensive crippling as a result of repeated hemarthroses and hemorrhages into the gastrocnemii. This patient, likewise, has been rehabilitated. For the first time in his life he has been able to do some remunerative work in his profession (commercial artist). Despite his incapacitation, he has been able to travel 80 miles (129 kilometers) to and from the hospital for his treatments.

During the period of study this subject had four hemorrhagic episodes. Two hemorrhages, one in an elbow and one in a knee, occurred after plasma had been withheld for four days for experimental purposes; the third, an ileofemoral hemorrhage,[1c] began during a week end about sixty hours after a plasma infusion, and required hospitalization. For these reasons, therapy was changed from three to four infusions weekly. The fourth episode occurred while the patient was without plasma for ten days when, because of jaundice, he was advised to remain at home. All except the ileofemoral episode were mild to moderate in severity and lasted about one week while plasma therapy was continued.

Because it was felt, after one year's observation, that this patient's hemorrhagic tendency could be controlled by repeated infusions of normal plasma, a bilateral open tenoplasty of the achilles tendons was performed to overcome abnormal plantar flexion consequent to old hemorrhages into the gastrocnemii. It was felt that this physical handicap interfered with the patient's gait and resulted in undue strain on the knees, thus predisposing these joints to trauma. Seven days after an uneventful operation the wounds began to ooze despite daily plasma infusions which reduced the clotting time to relatively normal levels. At this time, the patient was slightly febrile and the wounds had partially separated. Because infection was suspected, the patient was given full doses of sulfadiazine and 300,000 units of penicillin with a daily plasma infusion for one week. Following the first dose of penicillin bleeding ceased and recovery was uneventful, the wounds healing by secondary intention. One hundred and fifty cubic centimeters of plasma was given daily for forty-two days and every other day thereafter. The operative result was good; the patient's gait is now greatly improved.

Case 3.—The third subject has also been much more active physically and socially, indulging in baseball, touch football, hunting, bowling, etc., for the first time in his life. He is experiencing his most sustained interval of uninterrupted school attendance, broken only by a severe infection of the respiratory tract requiring hospitalization and by one hemorrhage, described in the next paragraph. He, too, travels 80 miles three times weekly to receive plasma.

Despite many incidents of trauma there have been only three significant hemorrhagic episodes with no history of antecedent trauma. The first, sixty hours after a plasma infusion (over a week end) occurred into a knee and subsided within four days without requiring bed rest. The second, also into a knee, began about eighty hours after the last infusion of plasma (the patient failed to come in for his scheduled infusion of plasma because of icy road conditions). Incapacitation lasted about ten days, during which time the patient continued to receive plasma issued by us and administered daily at home by his local physician. The third hemorrhage, also into a knee, began seventy-two hours after a plasma infusion (over a week end) and subsided within three days while plasma therapy continued.

Case 4.—This subject has also been relatively free of significant hemorrhagic episodes despite greatly increased physical activity and many traumatic episodes, one occurring on a day when the patient was scheduled to receive plasma, consisting of a deep long laceration of the hand requiring hospitalization. Restriction of play at home and in school have been largely eliminated.

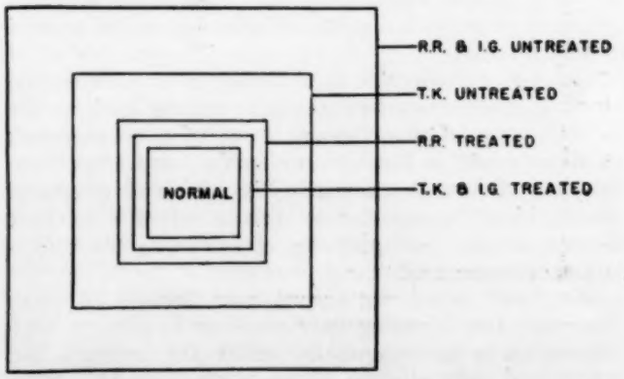

Fig. 3.—The over-all reduction in coagulation time induced by regularly administered normal plasma to persons with hemophilia. The areas enclosed by the rectangles represent the clotting time over the study period, integrated from the curves in figure 1.

It is practically impossible to record all the minor hemorrhages and ecchymoses which a hemophiliac patient ordinarily experiences during the course of his disease. These are so many and frequent that the usual patient pays little attention to them. During the course

of plasma therapy the subjects were unanimous in their opinion that they experienced markedly fewer minor hemorrhagic phenomena despite a pronounced increase in activity. With every lapse in plasma therapy the lesser hemorrhagic phenomena reappeared.

Control of the disease, as well as the disease per se, required numerous social and psychiatric readjustments. These will be described in a separate communication.[12]

Ten reactions to plasma were observed, an incidence of 1.2 per cent. Six were minor, characterized by urticaria or momentary faintness and giddiness. One, moderately severe, occurred early in the course of the study after the administration of a specimen which was not previously filtered.[13] Of the remaining three one was severe, associated with drop in blood pressure, dyspnea, distressing cough and severe headache, and two were moderate, producing chills, malaise, and transient fever. The incidence of reactions was no greater toward the end than at the beginning of the period of therapy.

One subject (I. G.) experienced insidiously developing jaundice associated with malaise, severe anorexia, mild epigastric distress and discomfort in the right upper quadrant. Physical examination revealed no abnormality except for jaundice and definite tenderness to palpation and percussion in the right upper quadrant and over the right lower costal border anteriorly. The icteric index was 67. After ten days at home, sixteen days after onset, the patient returned for plasma therapy, definitely improved and free of symptoms. At that time, his icteric index was 36, and three and one-half weeks later it was 14. We consider this a probable episode of mild "homologous serum jaundice."

COMMENT

Although transfusion with blood or plasma is generally accepted as being effective in the treatment of acute hemorrhage in hemophilia, no therapeutic plan has until now been devised which will control the hemorrhagic tendency over a prolonged period. On the basis of our observations we believe that frequent infusions of normal plasma are effective in the control of this disease.

There is considerable uncertainty as to whether the bleeding tendency of hemophilia is related solely to the delayed coagulation or also to some other factors such as disturbances in function of capillary and larger vessels in response to trauma. The beneficial effects of normal blood or plasma may also be referable to other factors besides their property of hastening the coagulation of hemophilic blood.

We have noted, in accord with numerous other observers, that bleeding may continue in persons with hemophilia when coagulation times are reduced and maintained only slightly above normal levels. After bleeding has proceeded for some time, reduction to relatively normal clotting time may, in some cases, fail to induce prompt hemostasis. This may be related to hemophilia per se or to local infection, as is suggested by the dramatic response to penicillin[14] in cases 1 and 2. Continuation of bleeding despite reduction in clotting time should be differentiated from initiation of new hemorrhages. In the latter the effect of vasoconstriction of the injured blood vessel exerts its fundamental role in the over-all hemostatic mechanism.[15] After several hours this important vascular reaction operates no longer.

Experience obtained in the use of heparin for delaying coagulation of blood in the treatment or prevention of phlebothrombosis and embolism indicates that a clotting time of between fifteen and twenty minutes is a relatively safe range within which untoward hemorrhagic phenomena are unlikely to occur,[16] although exceptions are occasionally encountered. Retarding coagulation by heparin to two to three times the normal is regarded as innocuous except in cases of active bleeding or within three hours following surgery. Even immediately after infusion of plasma the coagulation time of hemophilic blood is at best in the upper limits of normal, or, more often, slightly above normal (fig. 1). Under such conditions the person with hemophilia may be compared with a heparinized person having a similar coagulation time. That the latter will exhibit persistent bleeding if heparinization takes place too soon after surgical treatment or that he may experience spontaneous hemorrhage is perhaps of significance in explaining some of the hemorrhagic phenomena seen in hemophilia despite transfusions with blood or plasma.

Of fundamental importance is the question: Is the hemophiliac patient with a clotting time of ten to twenty minutes less prone to hemorrhage than one with a clotting time of thirty to one hundred and eighty minutes? The proved efficacy of blood or plasma transfusion in the therapy of acute hemorrhage in hemophilia supports an affirmative answer. The positive correlation between bleeding tendency and delayed blood coagulation induced by heparin also supports this view.

On the basis of experience with heparin it would seem desirable to maintain the clotting time of hemophilic blood at least below twenty minutes. As can be seen from figure 2 this can be done only by the administration of about 10 cc. of plasma every eight hours, 150 to 180 cc.[17] every twenty-four to thirty hours, or disproportionately greater amounts every forty-eight hours. The first method is not practical; the third seems inordinately wasteful of plasma in view of the rapid disappearance of the clot-promoting effect in vivo (fig. 2[18]). The dosage and frequency of administration which we employed were considered the most practical under the circumstances, although it was realized that the coagulation time would, and often did, exceed twenty minutes and that hemorrhage might accordingly ensue.

The isolation of thromboplastic and other clot-promoting elements from various biologic materials has been attempted. Excepting some derived from human plasma their intravenous use may be dangerous.

12. Cohen, E., and Herrman, R.: Social Adjustment of Six Patients with Hemophilia: Prior to and During Prophylactic Treatment, to be published.

13. We have observed that, after thawing, macroscopic "fibrin" shreds appear in the plasma which are removed by filtration through a stainless steel 150 mesh filter.

14. Although clot promoting properties have been reported for penicillin the antibiotic has been found ineffective as a clot accelerator in hemophilia (Macht, D.: Thromboplastic Properties of Penicillin and Streptomycin, Federation Proc. **6**: 160, 1947).

15. MacFarlane, R. G.: Critical Review: The Mechanism of Hemostasis, Quart. J. Med. **10**: 1, 1941. Quick, A. J.: The Hemorrhagic Diseases and the Physiology of Hemostasis, Springfield, Ill., Charles C Thomas, Publisher, 1942, p. 91.

16. Murray, D. W. G.: Some Experimental and Clinical Aspects of the Use of Heparin, Surg., Gynec. & Obst. **70**: 246, 1940; **72**: 340, 1941. Crafoord, C., and Jorpes, E.: Heparin as a Prophylactic Against Thrombosis, J. A. M. A. **116**: 2831 (June 28) 1941. Homans, J.: Venous Thrombosis and Pulmonary Embolism, New England J. Med. **236**: 196, 1947.

17. Less would be necessary for children, probably proportionate to the blood volume.

18. Alexander, B.: Studies on Hemophilia: III. Some Physiological and Biochemical Properties of the Antihemophilic Principle of Normal Human Plasma, to be published.

It is hoped that antihemophilic plasma fractions will replace whole plasma in the control of this disease. At present they do not show uniform potency.[10]

That the coagulation defect in our subjects did not become worse under plasma therapy is of the utmost importance. We found no evidence of refractoriness. This is in contrast to the result in the patient of Munroe and Jones [5] whose condition is reported to have become resistant to blood or plasma transfusion and whose blood was shown to contain an anticoagulant. Whether this development can be attributed to the use of frequent transfusions, as is claimed by the authors, or whether it appeared spontaneously, as is suggested in the case of Lawrence and Johnson,[19] is still uncertain.

Persistence of the coagulation defect after the therapeutic period, while throwing no definite light on the pathogenesis of hemophilia, suggests a fixed inability of the hemophiliac person to elaborate the antihemophilic moiety found in normal plasma.

Our finding of relative ineffectiveness of intramuscular administration is not in accord with other reports [6] of accelerated coagulation following injections of plasma or plasma "globulin" substance via this route. The discrepancy is perhaps related to differences in the assay methods and the amounts of materials used.

Since the effect of 50 or 100 cc. of plasma administered intravenously may not be distinguishable from that of 10, and 650 to 750 cc. may not be distinguishable from 150 to 190 cc., great caution should be exercised in comparing the antihemophilic potency of different biologic materials on the basis of their clot-promoting action in vivo. The ability to superimpose curves representing the degree and duration of clot acceleration in vivo may be an unreliable basis for drawing conclusions with regard to antihemophilic potency.

The hemorrhages experienced by our subjects, most of them occurring when the clot-promoting effects of the last administered plasma had largely disappeared, also attest to the value of continued repeated plasma therapy, since the hemorrhagic phenomena, coinciding with lapses in therapy, serve as a control for the therapeutic approach. It is probable, also, that minor hemorrhagic phenomena, such as were observed in our subjects after definite trauma and as might be expected on the basis of clotting times rising intermittently, were prevented from becoming major episodes by the frequent administrations of plasma. On the other hand, persistent bleeding, even when the clotting time is maintained between ten and twenty-two minutes and in the absence of infection, suggests that factors other than delayed coagulation of blood may be involved in the hemorrhagic phenomena of hemophilia.

The therapeutic method which we have used is admittedly laborious and cumbersome. It requires an efficient blood bank with a positive balance of blood. The sizeable dose of plasma and its relative ineffectiveness when given intramuscularly exclude nonintravenous routes of administration. The person with hemophilia becomes, furthermore, "tied" to a hospital institution. Nevertheless, we believe that the prophylactic management of hemophilia by means of plasma is not only effective but also feasible. Most hospitals have blood banks. The whole procedure can be entrusted to a blood bank nurse. Patients can be scheduled to appear three mornings a week in the outpatient department for their treatments. After five to ten minutes of infusion, the patient is free to leave.

The supply of veins has presented no great problem in the adult patient, although our subjects were repeatedly subjected to many additional venipunctures for experimental purposes. In some of the patients, furthermore, many veins had already been destroyed by previous blood transfusions and hemorrhages.

Against the benefits derived from plasma must be weighed possible ill effects such as reactions and the transmission of infectious diseases. Obviously, this danger would still exist when and if plasma fractions became therapeutically practical.

The incidence of reactions to plasma in our group was smaller than that reported by other observers,[20] although it should be pointed out that in our study each member of a small group received a large number of plasmas, whereas in other studies each recipient in a large group was given one, or perhaps several, plasma infusions. It is of interest that the incidence or severity of reactions was no greater toward the end than at the beginning of the study. We obtained no evidence that passive transfer of sensitivity to allergens from donor to recipient occurs.[20]

The absence of reactions attributable to incompatibilities between donor plasma and recipient red cells is probably due both to the small volume of each infusion and to the relative rarity of extremely high agglutinin titers.[21]

The frequent administration of plasma for the control of hemophilia raises the important question of the likelihood of transmitting serologic jaundice by this procedure.[22] The development of jaundice in 1 patient is of interest in this regard, although we cannot be sure that this was an episode of serologic jaundice. If we assume that it was, our figures [23] suggest that the incidence of infectiousness in the population at large is approximately 1 in 540 if the 3 other persons with hemophilia are considered still susceptible to the disease; of 1 in 130 [24] if they are excluded.[25]

SUMMARY AND CONCLUSIONS

The intravenous infusion of freshly processed, frozen, normal human plasma three to four times weekly provides a therapeutic approach to the effective control of hemophilia. On this regimen the status of 4 persons with hemophilia has been strikingly improved. The clot-promoting effect of plasma was constant over a period of twelve to twenty months. The underlying coagulation defect remained unaltered. The duration of the effect of normal plasma is related, but not proportionately, to the size of the dose. Intramuscular administration of plasma is relatively ineffective. The incidence of reaction was 1.2 per cent. No reaction could be attributed to incompatibility of blood groups. One patient contracted what was considered to be mild serum jaundice.

19. Lawrence, J. S., and Johnson, J. B.: The Presence of a Circulating Anticoagulant in a Male Member of a Hemophiliac Family, Tr. Am. Clin. & Climatol. A. **57**: 223, 1942.

20. Miller, E. B., and Tisdall, L. H.: Reactions to 10,000 Pooled Liquid Human Plasma Transfusions, J. A. M. A. **128**: 863 (July 21) 1945.

21. Aubert, E. F.; Boorman, K. E.; Dodd, B. E., and Loutit, J. F.: Universal Donor with High Titer Isoagglutinins: Effect of Anti-A Isoagglutinins on Recipients of Group A, Brit. M. J. **1**: 659, 1942.

22. Grossman, C. M., and Saward, E. W.: Homologous Serum Jaundice Following the Administration of Commercial Pooled Plasma, New England J. Med. **234**: 181, 1946.

23. The total amount of plasma injected into the four hemophiliacs was 121 liters, which were obtained from about 540 donors.

24. Calculated on the basis of the total number of donors who provided the plasma infused into this hemophiliac up to 4 months (presumptive incubation period) before the patient showed clinical jaundice.

25. Apparently susceptibility to serologic jaundice is not 100 per cent (Neefe, J. R.; Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious [Epidemic] Hepatitis, Am. J. Med. **1**: 3, 1946).

PHEOCHROMOCYTOMAS

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Tumors of pheochrome tissue have been considered to be among the rarer tumors, but with increasing interest in all types of hypertension and with improvements in diagnostic methods, these tumors have been recognized more frequently than formerly. The syndrome of "paroxysmal hypertension" that has been considered typical of tumor of pheochrome cells is familiar to all, but with the finding of more of these tumors observers now realize that many of them produce symptoms of persistent unremitting hypertension resembling the so-called essential hypertension. It has also been shown that some tumors arising from pheochrome tissue, notably the carotid body, apparently do not cause the hypertensive symptoms.

SYMPTOMS AND MANIFESTATIONS

The usual symptom complex is either spontaneous or induced and consists of a pounding headache, a pronounced beating of the heart with epigastric distress and a constriction of the hands and feet, often associated with a sense of impending death, lasting a few minutes to several hours. It is usually followed by excessive perspiration, weakness and exhaustion and sometimes shock. Associated with the attack is a decided rise in both systolic and diastolic blood pressure and a subsequent fall to the usual normal or lower levels at the termination of the attack. In addition, blood and urine examinations at the time of the attack show sugar curves somewhat similar to those seen in diabetes mellitus. It has been recognized that the attack is due to the effect of the release of an excess of a pressor substance, epinephrine, from the increased number of pheochrome cells in the tumor. At times death may result from the excess epinephrine released.

Continuous Hypertension.—It has been pointed out by Palmer and Castleman,[1] Howard and Barker [2] and Quinby [3] that a number of these cases do not present this typical intermitting syndrome but have a sustained continuous hypertension that when present has confused the observers so that for a long time the condition remains unrecognized. A number of times unsuspected tumors of the pheochrome tissues have been accidently discovered during the operative procedure of sympathectomy for continuous hypertension. The recognition that such continuous hypertension may be the result of a more or less continuous release of excess epinephrine is well illustrated by the following cases.

CASE 1.—J. L., a girl aged 12, was admitted Sept. 2, 1943 with a complaint of excessive perspiration and loss of weight for two years. She was intolerant of heat and refused covers even on cold winter nights. She complained of a fast beating heart and used only the slowest of movements because of her apprehension of her heart beating. She was excessively thin, with a moist skin, and showed a blood pressure of 210 systolic and 150 diastolic, which was lower when she was erect and higher when she was prone. Her basal metabolic rate was plus 50 to 65. From Sept. 2, 1943 to Aug. 16, 1944, she was studied in a number of admissions in which her various metabolic studies showed normal creatine-creatinine ratio and a reduced serum iodine (4.8 micrograms per hundred cubic centimeters; normal for her age, 6.2). The usual cold pressor tests showed immediate rise in blood pressure. Injection of 0.2 cc. epinephrine intravenously produced an immediate increase of her subjective complaints and increase in blood pressure. Her fundi showed a moderate degree of papilledema of disks with obliteration of disk margins bilaterally and increased congestion of the vessels. Auriculoventricular nicking was not noted. There were at first no hemorrhages or exudate. Results of a glucose tolerance test were within normal range, and she had no elevation of blood sugar or sugar in her urine. She showed no appreciable change under therapy with strong iodine solution U. S. P. Her true condition was finally suspected, and with an air insufflation roentgenogram a small tumor of the left adrenal was visualized. This was removed through a left flank incision on Aug. 16, 1944. She had the pronounced variations of blood pressure seen in these cases at the time of operation with a severe drop on removal of the tumor, but in a few minutes the blood pressure ascended again to high levels. Another tumor was then suspected to be present, and anteriorly in the incision there was revealed a mass in front of the pancreas. Since in all preceding cases the blood fell to normal or lower than normal levels and remained there, this immediate rise in blood pressure was thought to be due only

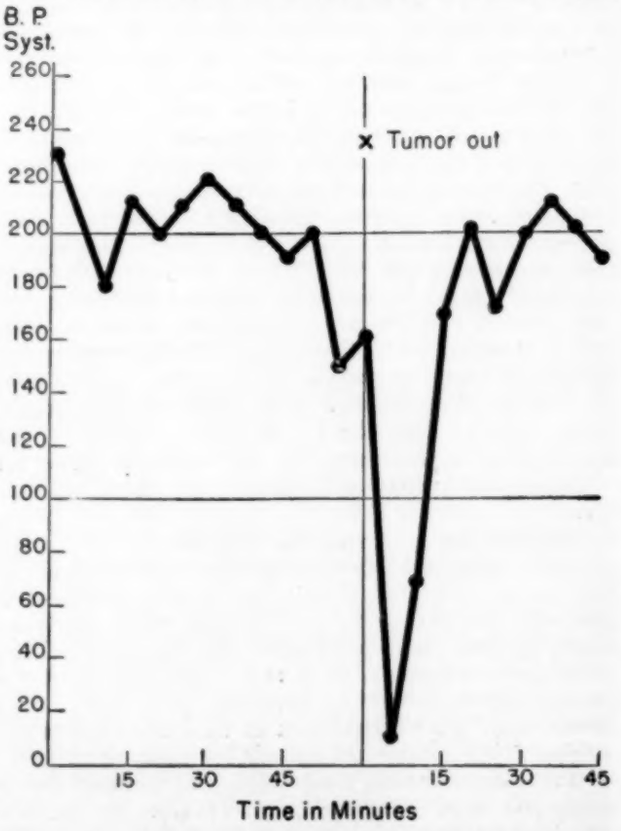

Chart 1 (case 1).—Systolic blood pressure taken at the time of first operation, showing the immediate drop in blood pressure on removal of the first tumor and the rapid rise to former levels due to the presence of the second tumor.

From The J. Bentley Squier Urological Clinic and the Department of Urology, College of Physicians and Surgeons, Columbia University.
Read before the Section on Urology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1947.

1. Palmer, R. S., and Castleman, B.: New England J. Med. **219**: 793, 1938.
2. Howard, J. E., and Barker, W. H.: Bull. Johns Hopkins Hosp. **61**: 371, 1937.
3. Quinby, W. C.: Tr. Am. A. Genito-Urin. Surgeons. **36**: 103, 1943.

to additonal excess pheochrome tissue elsewhere. The adrenal tumor microscopically was a pheochromocytoma.

She made a good recovery from the first operation, but her symptoms persisted. During this convalescence it was suggested that an epinephrine anatagonist (2-[1-piperidylmethyl]-1,4-benzodioxan) be used intravenously to determine whether

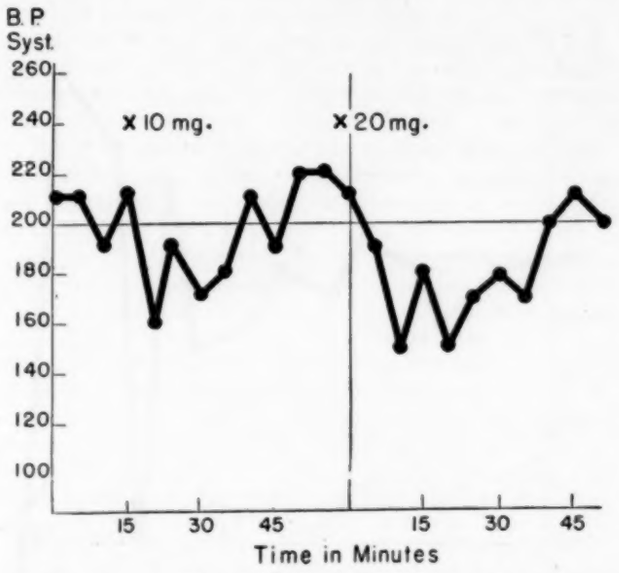

Chart 2 (case 1).—Effect of 10 mg. and 20 mg. of bendodioxane on the systolic pressure in the period before the second tumor was removed.

there was excess epinephrine in her blood. A significant fall in blood pressure was the result of the intravenous administration of the benzodioxan with a gradual rise to former levels. A number of injections were done, all with similar results. She was then again operated on and an extra-adrenal pheochromocytoma removed transperitoneally from the left preaortic area just superior to the pancreas. Immediately after the removal of the tumor her blood pressure declined to 110 systolic and 60 diastolic; it has remained around that level to date, with complete relief from all her former symptoms. She has gained weight back to normal for her age. Her metabolic changes returned to normal range and her retinal changes disappeared. The benzodioxan tests subsequent to removal of the tumor showed no alteration of the blood pressure.

This particular case was confusing because of the supposed rarity of these tumors in children and because a syndrome of continuous unremitting hypertension was presented. The presence of an intra-adrenal tumor was established by the air insufflation roentgenograms, and the failure of the blood pressure to remain low after removal of the first tumor made a second extra-adrenal tumor suspected. This was confirmed by the effect of the benzodioxan test, although, this being the first case in which the effects were registered, the value of the test had not been established.

Change to Sustained Hypertension.—The change in some of these cases from remittent to sustained hypertension is illustrated by the following cases.

CASE 2.—D. B., a girl aged 10, was admitted Feb. 20, 1946 with nervous attacks and excessive perspiration for three years. At first the attacks consisted of nervousness, shortness of breath, epigastric pain and nausea followed by profuse sweating, and they occurred about every two weeks. The attacks became more frequent, and at admission and during study she had no periods of remission. During hospital observation her blood pressure varied from 210 systolic and 160 diastolic to 185 systolic and 130 diastolic. She showed no physical changes except overaction of the heart. She was studied for thirty days, in which she showed no sugar in her urine and normal glucose tolerance readings. Her fundi showed changes similar to those in case 1 and according to the examiner[4] were seen in no other condition than that observed in the former case. A test with the benzodioxan similar to that done in case 1 showed a significant drop (50 mm. systolic plus) in blood pressure, which remained depressed for ten minutes. Repetition of the test produced similar results. Intravenous pyelograms showed normal nondisplaced kidneys, and air insufflation roentgenograms did not reveal an enlargement of either adrenal. A diagnosis of extra-adrenal pheochromocytoma was made. It was suspected to be in the upper part of the abdomen.

A transperitoneal operative exposure showed a retroperitoneal tumor at the bifurcation of the aorta (Zuckerkandl's body) and another large tumor in the epigastric area, retroperitoneal and covered with large cirsoid, dilated veins. The anterior veins were doubly ligated and cut. When attempts were made to separate the vena cava from the large tumor, there was pronounced increase in pulse and pressure and the pulsation suddenly ceased. Attempts at resuscitation failed.

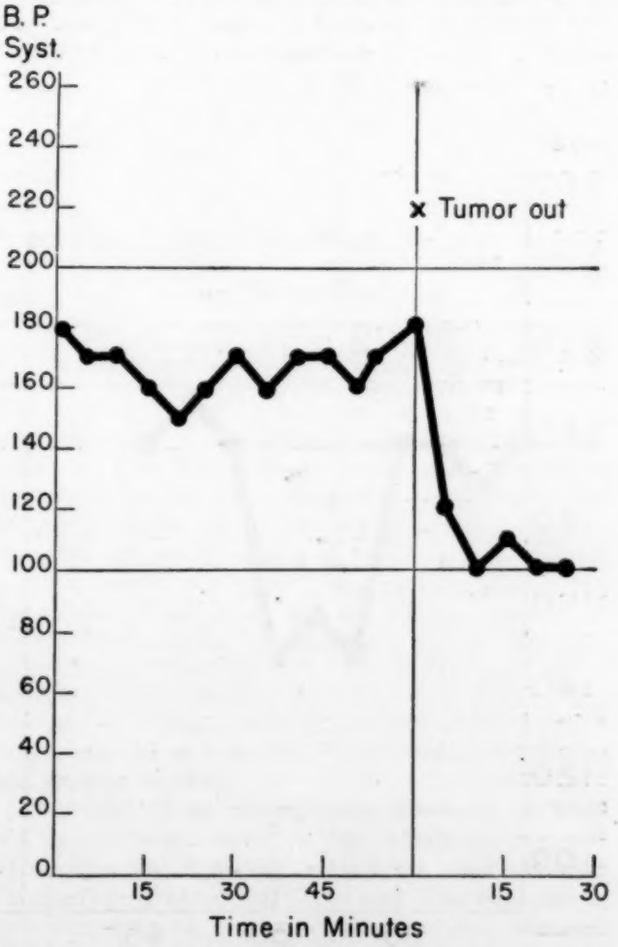

Chart 3 (case 1).—Systolic blood pressure taken during the second operation, showing the almost immediate drop to low level after removal of the second tumor. There was apparently no more excess epinephrine being secreted after removal of the tumor and the conclusion reached was that all secreting tumor tissue had been removed.

Injections of the benzodioxan given during the pronounced change in blood pressure had no effect.

An autopsy showed an extra-adrenal pheochromocytoma between the aorta and the vena cava, intimately attached to

4. Bruce, G. M.: Tr. Am. Ophth. Soc. 45: 1, 1947.

both and the size of an orange. A second pheochromocytoma at the bifurcation of the aorta, about the size of a small plum, was also found. Both adrenals and kidneys were anatomically normal. The patient had hypertrophy of the heart, atheromatosis of the aorta and coronary vessels, cysts of the ovaries and mild adenomyosis of the uterus. Nephrosclerosis was not present, a fact brought out by Howard and Barker, who wrote that if it was present it was only so in a mild degree.

This child showed the vascular changes seen with continuous hypertension, except for the supposed specific changes in the fundi. The air insufflation roentgenograms showed anatomically normal adrenals, but the air did not infiltrate around the epigastric tumor because of the tight fascial planes over the tumor. Infiltration of air around an extra-adrenal tumor so that it is visualized has apparently only been rarely seen and only when the fascial spaces are not under pressure and are connected with the perirenal area. This has occurred only once in our department.

This, the second case in which a significant reduction occurred in the blood pressure with injections of the benzodioxan, gave more significance to the test, especially so since no changes occurred in patients with

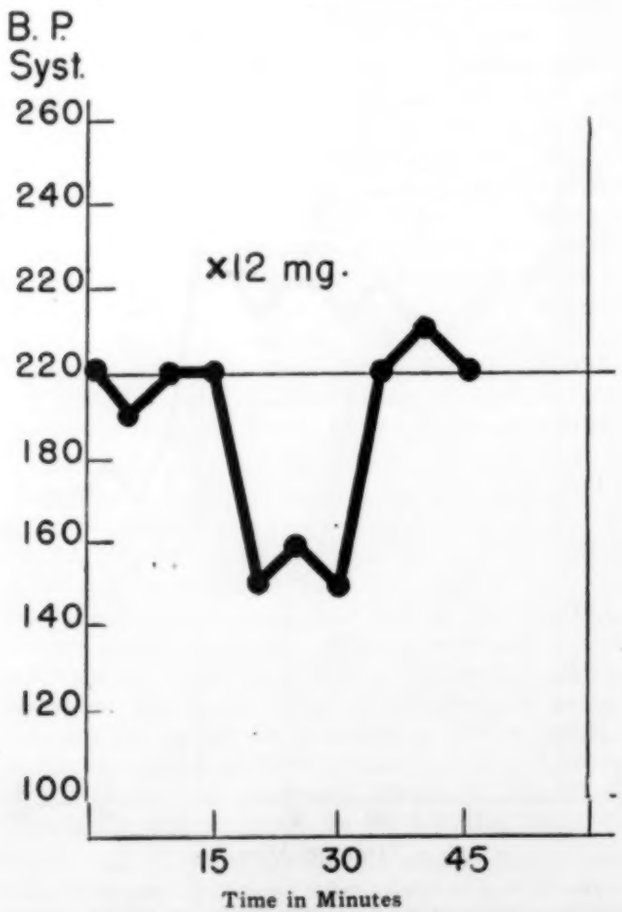

Chart 4 (case 2).—Effects of 12 mg. of benzodioxane on the systolic blood pressure.

known essential hypertension; in a number of patients suspected to have pheochromocytoma results of the tests were negative, and on operative exploration no tumors were found. The determining factor of the diagnosis was the positive reaction to the benzodioxan test with a history of a gradual change from paroxysmal hypertension symptoms to more or less continuous hypertension.

Retinal Changes.—The peculiar retinal changes in these 2 cases (separately reported by Bruce) Bruce stated that he had not seen before and definitely not

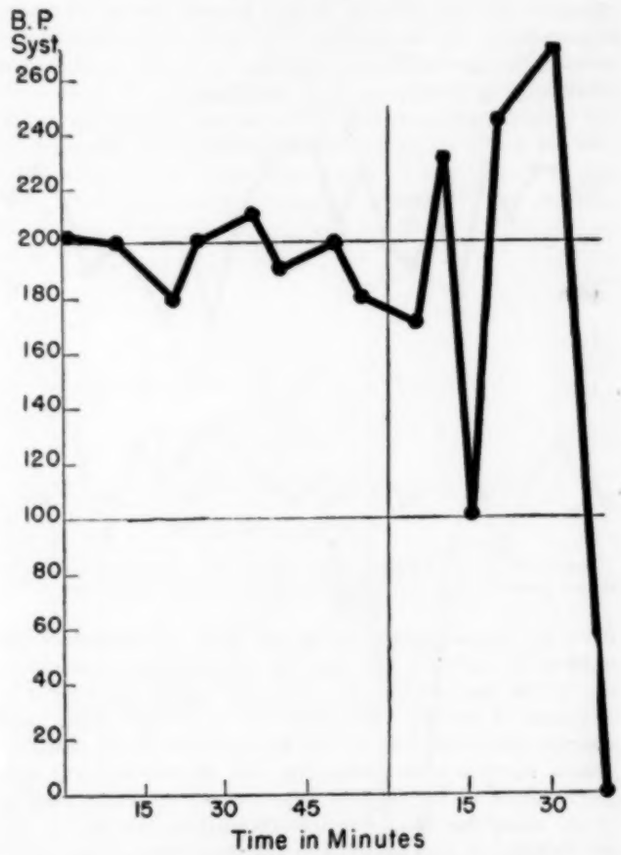

Chart 5 (case 2).—Systolic blood pressure recordings at operation, with extreme elevation on attempt to isolate and ligate the vessel to the vena cava and immediate fall to zero with the death of the patient.

in other cases of hypertension. The papilledema and disk margin blurrings with fluffy exudate and hemorrhage were next seen by him in a third case, and the patient was referred into the hospital with the diagnosis of suspected pheochromocytoma based on the eye examination alone, associated with hypertension.

Case 3.—P. D., a boy aged 11, was admitted Oct. 4, 1946 complaining of failure of vision for one week. The objects in the room were blurred and he was unable to read. He was examined by an ophthalmologist on the day of admission; (1) hypermetropia, (2) exudate in the retina and (3) hypertension were found. He had excessive sweating and thirst associated with a pounding headache, abdominal pain and nausea and vomiting and a pounding heart beat for three years. These attacks occurred at intervals, precipitated by excitement or activity; they usually occurred every month or so, lasted a day, and were followed by diaphoresis, weakness and loss of appetite. Blood pressure readings in between the attacks were reported as normal.

He was a healthy-appearing boy, somewhat apprehensive. His blood pressure was 260 systolic and 190 diastolic. A severe pounding headache developed, with pallor, sweating, nausea and vomiting and with a pulse rate of 150 and blood pressure of 270 systolic and 210 diastolic. The attack lasted

two days with listlessness following. A test with the benzodioxan after the attack showed a drop of blood pressure to 138 systolic and 110 diastolic, lasting only a few minutes. His pressure slowly fell in three days to 118 systolic and 82 diastolic. Air insufflation roentgenograms showed the left adrenal and kidney normal in size and position. The right kidney was small and poorly delineated by the air, and there was no infiltration at the hilus. The left adrenal looked normal. Intravenous and retrograde pyelograms showed lessened secretion in the right kidney diagnosed as "hypoplastic." While under observation he improved clinically and his eye-ground changes regressed. At no time did he show sugar in his urine, increase in sugar in his blood or abnormal sugar tolerance reaction. By the twenty-third day his improvement was pronounced, with normal blood pressure; he was able to read and was up and about.

He was operated on Oct. 29, 1946 under tribromoethanol-nitrous-oxide-oxygen anesthesia, and a transverse incision was made. A tumor about the size of a peach mesial to the hilus of a hypoplastic right kidney was removed with the kidney. The right adrenal was normal. During the entire procedure the blood pressure remained relatively stable and exhibited no untoward rise or decline. His recovery was excellent, his blood pressure remaining around 120 systolic and 80 diastolic, and his retinal changes regressed. On the ninth day another trial of the benzodioxan was given (0.6 Gm.), with no significant

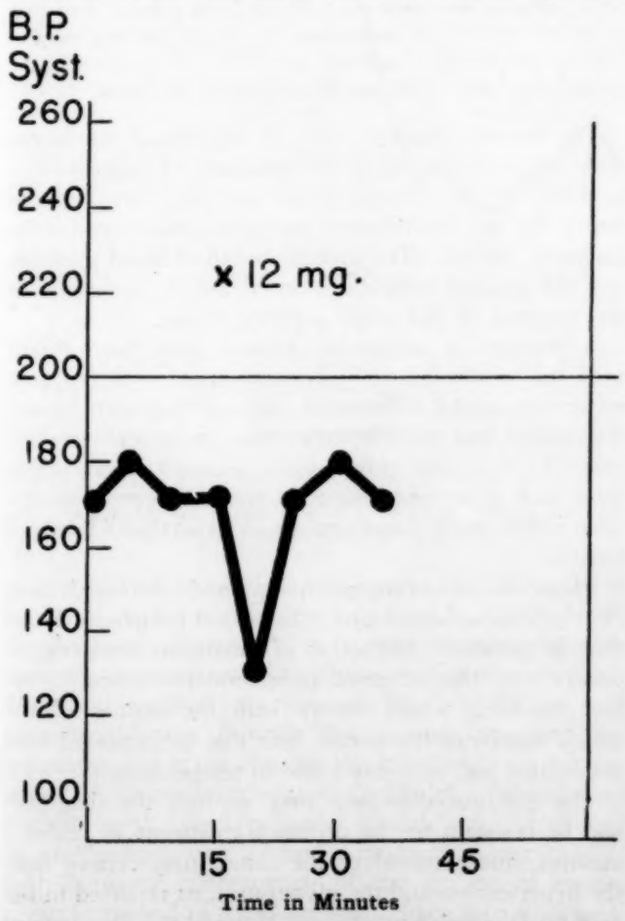

Chart 6 (case 3).—Effect of 12 mg. of benzodioxane on the systolic blood pressure.

rise or fall after the administration of the drug. The pathologic report was (1) pheochromocytoma of aberrant adrenal medullary tissue, (2) hypoplasia of the right kidney and (3) calcium deposits in the right kidney. The tumor showed pronounced degenerative changes throughout, due to infarction caused by thrombosis in the main artery to the tumor.

From these 3 cases, the following inferences may be drawn, if such inferences are permissible: The syndrome occurs in children more often than shown by the few cases reported. The continuous hypertension phenomena may be seen oftener in children, and

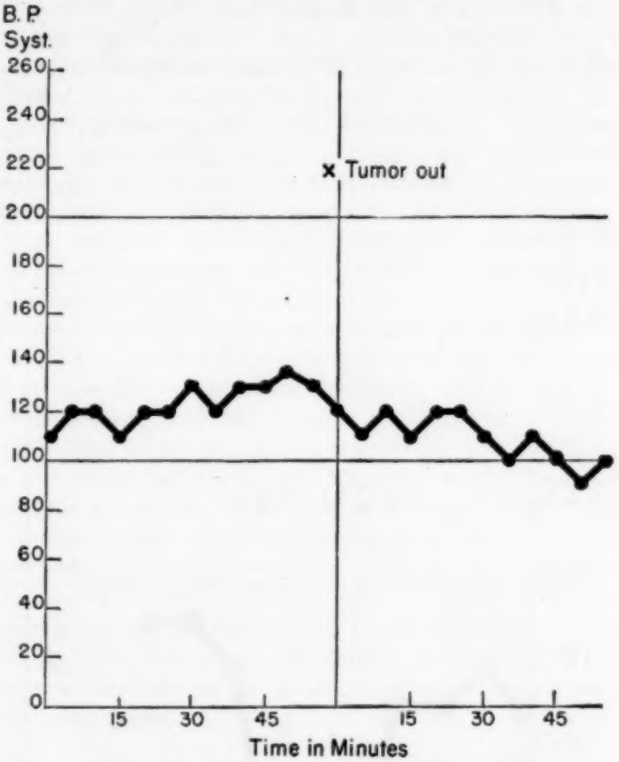

Chart 7 (case 3).—Systolic blood pressure recordings during operation. The patient had spontaneous infarction of vessels to the tumor, with amelioration of the symptoms previous to operation, and as a result there was little change during operation and following removal of the tumor.

when they occur they may be associated with characteristic retinal changes. In children changes in metabolism occur but changes in blood sugar and urine resembling diabetes are not so frequent (at least they did not occur in any of these 3). In children multiple tumors may occur; on removal of one tumor the failure of the blood pressure to stay within low records should make an additional tumor suspected. In these 3 children five tumors occurred; only one of these was intra-adrenal; the other four were extra-adrenal. A spontaneous infarction occurring in 1 patient relieved all symptoms, so that operative removal was without incident.

The usual tumor is seen more frequently in adult life, occurs more often in the female (our cases: 10 females and 4 males). They are usually benign (McKeith [5] indicated that 9 per cent were malignant), and according to McKeith [5] they are 9.7 per cent bilateral.

The tumors are mostly seen intra-abdominally. In 1 case the tumor was reported to be intracranial.[6] In 3 cases tumors have been reported as intrathoracic; one tumor was successfully removed by Mayer.[7] Multiple tumors occurred in our cases 3 times in 14. The patient whose thoracic tumor was successfully removed

5. MacKeith, R.: Brit. Heart J. **6**: 1, 1944.
6. Cahill, G. F.: Surgery **16**: 233, 1944.
7. Mayer, H.: Personal communication to the author.

by Mayer still has some symptoms of excess epinephrine, but my co-workers and I were able to demonstrate normal adrenal shadows by air insufflation roentgenograms.

BASES FOR DIAGNOSIS

A diagnosis of pheochromocytoma depends on (1) a typical attack and associated clinical findings, among which may be characteristic retinal changes in children; (2) evidence in a case of so-called essential hypertension of symptomatic and clinical findings characteristic of the phenochromocytoma syndrome; (3) demonstration in the blood of a pressor substance as

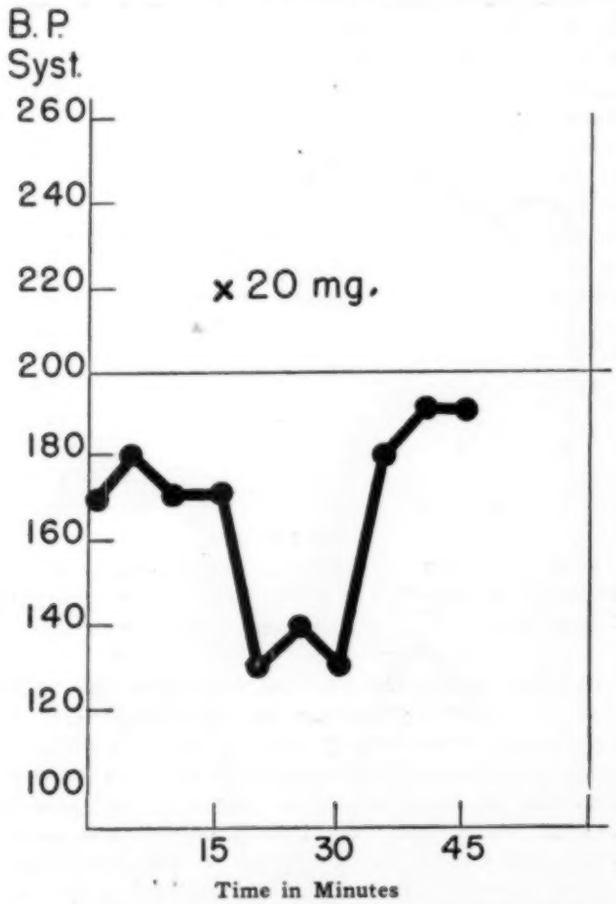

Chart 8 (case 4).—An adult with a large tumor and paroxysmal type of hypertension. Effects of 20 mg. of benzodioxane on the systolic blood pressure.

shown by Beer, King and Prinzmetal[8] or a significant reduction in the blood pressure associated with the intravenous injection of an epinephrine antagonist as the benzodioxan series; (4) precipitation of an attack in a resting stage by an epinephrine-producing stimulus as described by Roth and Kvale[9]; (5) roentgenographic evidence of the presence of a tumor, either without or with perirenal air insufflataion or by renal displacement with pyelographic mediums.

The use of the various steps in the diagnosis are illustrated by the following typical case.

CASE 4.—K. G., a woman aged 42, was admitted on Feb. 7, 1947 with hypertension and hyperthyroidism of one year's standing. She had attacks of headache, heart pounding, epigastric distress and pronounced sweating. These attacks were associated with hypertension (220 systolic and 130 diastolic) and glycosuria. The eyegrounds showed slight sclerosis of the retinal vessels with a slight haziness of the temporal margin of the left disk. These were seen by the same ophthalmologist who had seen the retinas of the children and were not characteristic of pheochromocytoma. Her basal metabolic rate was + 23 per cent. The fasting blood sugar was 153 mg. per hundred cubic centimeters and nonprotein nitrogen 24 mg. Phenolsulfonphthalein excretion was 80 per cent in two hours. The serum sodium was 140.7 mg. The benzodioxan test showed a fall of blood pressure to 135 systolic and 80 diastolic, with a rise gradually in fifteen minutes to the level before injection. The intravenous pyelograms showed a normal pair of kidneys with increased motility. The air insufflation roentgenograms showed an ovoid tumor above the right kidney in the area af the right adrenal.

Through a transverse epigastric incision a pear-shaped tumor of the right adrenal was removed transperitoneally. There was the pronounced elevation of the blood pressure on ligation of the blood supply without handling of the tumor, as usually seen, and a rapid fall following removal. Epinephrine slowly administered intravenously gradually raised the systolic blood pressure from 60 to 100 in eight hours. Since removal of the tumor, after an uneventful recovery, her blood pressure remained on the average of 120 systolic and 80 diastolic for two months. At that time her basal metabolic rate was — 5 per cent and she occasionally had a small amount of sugar in her urine.

The history characteristic of the classic syndrome with the establishment of presence of excess epinephrine by the antagonist and the delineation of the tumor by air insufflation roentgenograms made the diagnosis certain. The immediate fall of blood pressure and the gradual return to normal are characteristic of the removal of the usual solitary tumor.

A number of metabolic changes have been found with the syndrome. Hypermetabolism is of frequent occurrence and a differential diagnosis between hyperthyroidism and pheochromocytoma is sometimes difficult. In 1 of our children the lessened blood iodine level and poor response to administration of potassium iodide made the diagnosis of hyperthyroidism not tenable.

Elevation of serum potassium and increased urea clearance have been found. Increased peripheral blood flow is present. Reduction of cutaneous temperature occurs with the increased peripheral resistance. Profuse sweating which occurs with the ending of the attack dissipates the excess heat due to increased heat production and prevents a rise in temperature.

The glycosuria present may confuse the diagnosis and be resistant to the ordinary treatment of diabetes mellitus, and removal of the tumor may relieve both the hypertension and the glyscosuria, as reported in the case by Duncan, Semans and Howard.[10] This patient was older than the usual patient. We have noticed that the sugar changes occurred as the patients were older. In the 3 children reported on in this paper, the usual changes in blood sugar and urine were not associated with the syndrome. One patient (our

8. Beer, E.; King, F. H., and Prinzmetal, M.: Ann. Surg. **106**: 85, 1937.

9. Roth, G. M., and Kvale, W. F.: J. Lab. & Clin. Med. **30**: 366, 1945.

10. Duncan, L. E., Jr.; Semans, J. H., and Howard, J. E.: Ann. Int. Med. **20**: 815, 1944.

case 4) had glycosuria after removal of the tumor with abatement of all other symptoms.

Hysteria and psychoneurosis may present difficulties in determining whether a pheochromocytoma is present, as has been pointed out by Van Epps [11] and myself. In spite of failure to find positive evidence of excessive epinephrine by the benzodioxan test and although the adrenal glands appeared normal in air insufflation roentgenograms, when there were a suggestive history and simulated attacks exploration was done in a number of these cases in the hope of finding an extra-adrenal pheochromocytoma. The failure to observe a tumor gave us increased confidence in the benzodioxan test.

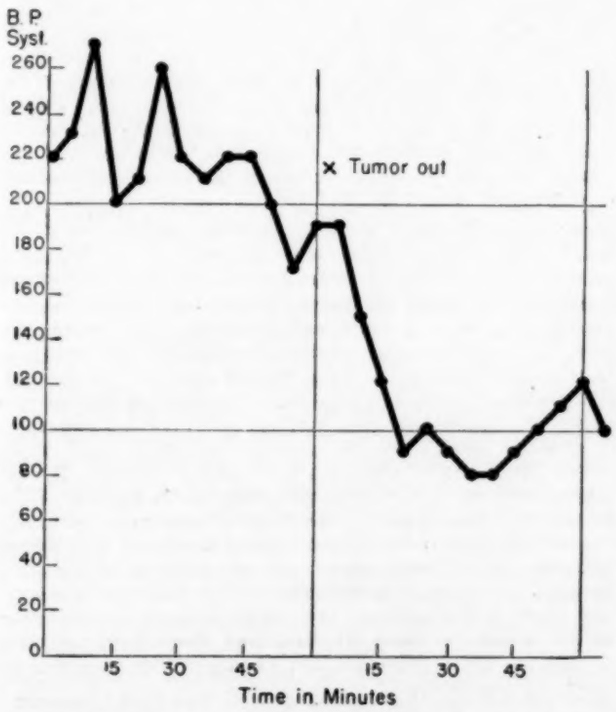

Chart 9 (case 4).—The systolic blood pressure recordings during operation. There was a rise in blood pressure on ligation of the tumor vessels and a pronounced fall to low levels after removal. This is the more frequent recording seen and occurs with solitary tumors.

The use of benzodioxan derivates as indicators of excess epinephrine was first suggested by Goldenburg, Snyder and Aranow.[12] A simple method for this determination was sought because the use of a modified Pissemski method as reported by Beer, King and Prinzmetal [8] was difficult and cumbersome and the apparatus and material available only in certain laboratories. A simple intravenous injection of a benzodioxan derivate with blood pressure studies was introduced by Goldenburg, Snyder and Aranow [12] in our case 1, with apparent confirmation of the finding of excess epinephrine and of the diagnosis. Since then they have shown that the blood pressure level in patients with "essential hypertension" is not influenced by the injection of the drug and that all other simulating syndromes showed no changes in blood pressure. They also showed that in the 4 proved cases of syndromes due to pheochromocytomas the fall in blood pressure following the injection of the drug was significant and of diagnostic importance and that it apparently occurs only with excess secretion of epinephrine, and that in the 3 surviving patients no changes occurred in the blood pressure postoperatively after injection of the drug.

The histamine test was described by Roth and Kvale,[9] who observed that intravenous injection of 0.05 mg. of histamine could immediately precipitate a hypertension crisis in a patient with pheochromocytoma. This we have not experimented with, because the recent positive cases were too serious to risk and that the diagnosis was established otherwise. We have, however, used the histamine test in those cases in which the reaction to the benzodioxan test was negative in order to have a double check, and in not any of such cases was the histamine test positive in result.

The use of air insufflation roentgenograms has been a safe and reliable indicator when the tumor is of the adrenal gland, and it is most satisfactory with small adrenal tumors that can be localized by no other method. Attempts made to delineate extra-adrenal tumors by fascial insufflation have not been very successful, having shown only one at the bifurcation of the aorta. The sealing of the fascial planes around the other tumors prevented the air from disseminating and outlining them.

TECHNIC

There has been a lowering of the mortality rate in surgical therapy of these tumors. The use of tribromoethanol in anesthesia induction has avoided precipitation of an attack. Epinephrine and adrenal cortical hormone should be available at operation and used if needed both during operation and afterward. One patient of ours with Cushing's syndrome and pheochromocytoma required cortical hormone subsequent to operative removal because of acute cortical adrenal deficiency after operation. Blood pressure readings are necessary almost continuously during operation. With multiple tumors the transperitoneal route has been more frequently used by us, although a high lumbar approach may be satisfactory for adrenal tumor. The handling of the tumor has been dangerous and should be reserved until all the vessels surrounding and connected with the tumor are ligated. The situations of some tumors make handling of the blood supply difficult and in some, such as our case 2, in a child with a large tumor between the vena cava and the aorta, temporary occlusion of the vena cava above and below the tumor may be necessary to prevent the escape of a lethal dose of epinephrine into the circulation. The use of the benzodioxan in that case in the small amount employed was without avail, probably because of the large amount of epinephrine released.

Following removal of a secreting tumor the immediate fall in blood pressure may be alarming. Intravenous administration of epinephrine has satisfactorily controlled this drop. A return to normal has been the

11. Van Epps, E. F.; Hyndman, O. R., and Greene, J. A.: Clinical Manifestations of Paroxysmal Hypertension Associated with Pheochromocytoma of Adrenal, Arch. Int. Med. **65**: 1123 (June) 1940.
12. Goldenburg, C.; Snyder, H., and Aranow, H., Jr.: J. A. M. A. **135**: 971 (Dec. 13) 1947.

usual result when all the excess epinephrine tissue has been removed. A rapid elevation of the systolic blood pressure in ten minutes or less following removal of the tumor and the elevation to near its former levels in our experience is an indication that a second tumor is present.

The postoperative care has been the one of combating an apparently depleted epinephrine state with accompanying low blood pressure. This has been successful with intravenous infusions with epinephrine. Studies of sodium and potassium balance showed only in 1 case a change suggestive of cortical depletion and that was in a case with associated mild Cushing's disease.

Most of these tumors are benign and unilateral; MacKeath's review, as stated before, indicated that 9 per cent were malignant and 9.7 bilateral. In 9 of his reviewed 165 cases there was an associated cutaneous neurofibromatosis, and these tumors were all bilateral.

In 2 of our 14 cases there were presumed to be metastases and the tumors were considered to be malignant. Attempts made by Masina [13] to grow our recent tumors in the anterior chamber of the eye of rodents has been unsuccessful. All tumors seen by us were of chromofin and ganglion cells. They contained abnormal amounts of epinephrine by assay, and the abnormal amounts were demonstrated as present in the tissue by staining methods.

SUMMARY

Pheochromocytomas occur mostly in the adrenal but do occur in other pheochrome tissue. The syndromes are due to excess epinephrine released into the blood. They may give typical syndromes of paroxysmal hypertension or may resemble essential hypertension. They may occur at any age, and the tumors may be multiple. The steps in the diagnosis are illustrated, and the diagnosis is often certain.

ABSTRACT OF DISCUSSION

Dr. Earl E. Ewert, Boston: That Dr. Cahill and his group should receive the gold medal for their classic work is no surprise. His experience with adrenal tumors extending over some twenty-five years has generated in all the appreciation that this one sort of rarity is more common clinically than has been suspected. The food for thought that he has offered is that persistent hypertension may be present in adrenal tumors and this more commonly in children; that a normal glucose tolerance range may be present and that sugar is absent from the urine and there is no elevation of the blood sugar; that adrenal chromaffin tumors may be multiple and extrarenal; that removal of a single chromaffin tumor without relief indicates the presence of an extrarenal tumor. Other observations that my associates and I have made in a small series are: In every patient with peculiar vasomotor paroxysms the possibility of a pheochromocytoma must be investigated. All hypertensive patients undergoing sympathectomy should have besides their normal routine urograms some of the specific diagnostic tests. Also, patients with typical epileptiform seizures should be considered as possibly having chromaffin tumors. A "mecholyl bromide" test is added to those that have already been given and to the new test that Dr. Cahill mentioned, the dioxan test. The "mecholyl" test consists of administering 25 mg. of the drug subcutaneously after a period of rest to obtain a stabilized blood pressure and pulse rate. The blood pressure and pulse rate are then recorded after "mecholyl" is given at one minute intervals, until they return to normal, in fifteen or twenty or thirty minutes. A positive reaction is shown by a decided rise in systolic and diastolic pressures. In the case tried, there was a rise of 106 mm. of systolic blood pressure and 60 mm. of diastolic blod pressure above the resting level following a preliminary fall lasting about one minute. The pressure returned to normal in fifteen minutes. Associated with the rise in blood pressure were all the symptoms characteristic of a paroxysmal attack of hypertension due to a chromaffin tumor. In addition, the patient experienced the side reactions of "mecholyl," which include nausea, asphyxia livida, sweating and dyspnea, which may be controlled by the administration of atropine. The controls were tried in 27 additional patients, ages 20 to 60; 7 were normal and 20 had hypertensive vascular disease. In the 27 controls, the reaction was positive in all, and of the 22 patients in whom the cold pressor test was performed, 17 showed a normal response and 5 showed a rise of more than 20 mm. and may be considered as hyperreactors. Of the 9 patients in this group on whom histamine was tried, 5 had a rise in blood pressure of 20 mm. or more and are considered as hyperreactors. During operation the sharp drop in diastolic pressure is the point at which the patient may be lost. This is the crucial point. The operation for pheochromocytoma is delicate; the internist and the anesthetist must be conscious of the catastrophe which may occur suddenly in manipulation of the tumor, even when ligation of the vessels has been taken care of before removal of the tumor and when one thinks that he has been especially careful not to manipulate the tumor and discharge amounts of pressor substance into the blood stream.

Dr. Seymour F. Wilhelm, New York: About fifteen years ago, Dr. Cahill discovered that the injection of air or gas into the perirenal space was of great aid in visualizing the larger adrenal tumors. However, in the delineation of the normal adrenal gland, the lesser enlargements, and the smaller tumors, my associates and I have found the simple roentgenogram following perirenal insufflation disappointing. We have been unable definitely to make up our minds as to the size of the adrenal gland or the absence or presence of any enlargement. We looked for other methods and tried laminography, by means of which a definite section of the body can be localized and the tissues above and below eliminated or blurred. By this means, we have been able to get rather sharp pictures of the normal adrenal and also of the lesser enlargements. I would like to ask how much adrenal gland tissue can be resected from the human being without causing Addison's disease. I have a female pseudohermaphrodite who had hyperplasia of both adrenals from whom I successfully resected the entire left adrenal gland, weighing 21 Gm., and about half the other adrenal. I would appreciate Dr. Cahill's telling us something about his experiences.

Dr. George F. Cahill, New York: I want to congratulate Dr. Wilhelm for going on with his laminographic work, which is really good. He has developed the simple thing that we had started with and carried on and has really advanced the outlining and the interpretation of these films definitely. As far as the amount of adrenal tissues to remove, that is difficult. One can take out one adrenal completely, but when one resects an adrenal, it is difficult to handle the hemorrhage. For the part of the adrenal left one does not know how much blood supply has been disturbed; there may be thrombosis; all the adrenal tissues may be killed. Of course, there are accessory adrenals known as Marchand bodies, occurring anywhere from the adrenal to the gonad. Tumors have occurred of these, not of the adrenal itself, with cortical syndromes characteristic entirely of the adrenal cortical syndrome. However, one cannot be sure that a particular patient will have some more Marchand bodies. I do not know yet how much adrenal to take out. I err on the side of leaving some in. The pheochromocytoma is extraordinary. The whole thing is dramatic. It is the only hypertension that one cures the cause of. One can now definitely cure it with apparent safety with the exception of that ten minutes of handling the tumor. Once the surgeon gets past that point, usually he is all right. The patient goes on; some patients have cortical deficiency following the handling of the tumor, but the deficiency can be corrected. We had 1 patient that had both a Cushing syndrome and a pheochromocytoma in the same adrenal, so that the deficiency subsequent to the operation was cortical deficiency and we had to treat it like an addisonian crisis.

13. Masina, M. M.: Personal communication to the author.

TREATMENT OF ADVANCED MAMMARY CANCER WITH TESTOSTERONE

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and
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The purpose of this paper is to present the results in 20 consecutive cases of advanced mammary cancer in which testosterone propionate was used. The minimum observation period is one year.

Ulrich [1] (1939) was the first to describe testosterone therapy in advanced mammary cancer. Although the doses were too small to produce chemical castration, his 2 cases showed a favorable response. Loeser,[2] in the same year, reported 2 patients, who had recurrent mammary cancer, treated with testosterone for menorrhagia. They lived for eighteen months without further recurrence. It was not stated whether or not recurrence was present at the beginning of testosterone therapy. Prudente [3] used testosterone prophylactically following mastectomy in doses adequate to produce ovarian suppression.

So far as we can determine, 92 cases of advanced mammary cancer treated with testosterone have been recorded in the literature; in addition, Prudente [3] has studied the prophylactic effect in 63 cases and Snapper [4] has treated 29 patients prophylactically with combined castration (surgical or with roentgen rays) and testosterone. In January 1948, Adair [5] wrote that 450 patients had been treated and observed by his group; 233 treated for advanced cancer and 217 treated prophylactically following radical mastectomy. Of the group with advanced cancer, 28 cases of advanced cancer have been reported in the literature up to the present writing.

Isolated favorable results in advanced cases have been reported.[6] These include cases of both soft tissue lesions and skeletal metastases. In Snapper's [4] 29 cases, castration (either surgical or with roentgen rays) combined with testosterone therapy did not protect against the subsequent development of distant metastases in cases with axillary involvement at the time of operation. Prudente [3] reported that in his 63 patients treated with radical surgical intervention and testosterone, the instances of three, four and five year survivals were increased by approximately 100 per cent as compared with a series treated with surgical intervention alone.

TESTOSTERONE

The property of testosterone for increasing the retention of sodium and potassium has been well established (Thorn and Engel,[7] Kenyon and his co-workers [8]). In addition, Kenyon and his co-workers [8] and Abels, Young and Taylor [9] have demonstrated increased protein nitrogen retention. Kenyon and his colleagues [8] treated 4 eunuchoid persons with testosterone propionate and observed a gain in weight due largely to water held in association with the sodium and nitrogen. Butler, Talbot and MacLachlan [10] concluded from their studies that potassium was retained primarily in the tissue fluids. The electrolytes and nitrogen retain water; consequently a gain in weight occurs. The increased weight is lost rapidly following cessation of treatment. Thorn and Engel [7] noted that decided diuresis and loss of weight occurred seventy-two hours after testosterone therapy was stopped. In addition, there was increased excretion of sodium, chlorides, potassium, inorganic phosphorus and total nitrogen. Thus, the evidence indicates that the electrolytic effect, in association with the protein nitrogen retention, is responsible for a transient rather than a permanent gain in body weight. For these reasons, a gain in weight *per se* does not necessarily indicate a favorable influence on the disease. This effect was observed clinically in several patients in whom peripheral edema developed while they were receiving testosterone. It is for this reason that testosterone must be used cautiously in patients with cardiac disease.

The changes in blood calcium and blood phosphorus during testosterone therapy are not well understood, and there is a decided divergence of opinion in the literature. Adair [6f] has described decided reduction in the serum calcium level in patients with metastasis to bone and has interpreted this decrease as evidence of calcium deposition in bone or a cessation of osteolysis. In none of his reported cases which responded favorably was there a change in the serum calcium which could be interpreted as significant. Snapper [4] reported 29 patients treated with castration and testosterone and noted no significant change in the serum and phosphorus. Farrar and Woodard [6e] treated 33 patients with smaller doses of testosterone and reported an increase in serum calcium in some cases. Adair and Herrman [6g] have noted that in patients with decidedly elevated serum calcium the condition of the patient is aggravated by testosterone therapy, and they have intimated that the drug should not be used under those conditions. While this, in general, is true, we have recently seen a patient with an elevated level of serum calcium who showed no untoward effects following administration of large doses of testosterone propionate. The level of the blood phosphorus has not proved to be of value in the evaluation of testosterone therapy.

Alkaline phosphatase is present where there is osteoblastic activity. This osteoblastic activity may be either reparative following osteolytic metastases or it may

From the Chicago Tumor Institute.
Dr. Schlemenson is a trainee of the National Cancer Institute.
The testosterone propionate ("oreton") used in this study was made available by the Schering Corporation, Bloomfield, N. J.

1. Ulrich, P.: Testosterone et son role possible dans le traitment de certains cancers du sein, Acta. Union internat. contre cancer **4**: 377, 1939.
2. Loeser, A. A.: Male Hormone in the Treatment of Cancer of the Breast, Acta, Union internat. contre cancer **4**: 375, 1939.
3. Prudente, A.: Postoperative Prophylaxis of Recurrent Mammary Cancer with Testosterone Propionate, Surg., Gynec. & Obst. **80**: 574, 1945.
4. Snapper, I.: Castration Combined with Testosterone Treatment After Mastectomy for Breast Cancer, J. Mt. Sinai Hosp. **14**: 618, 1947.
5. Adair, F.: Testosterone in the Treatment of Breast Cancer, M. Clin. North America **32**: 18-36, 1948.
6. (*a*) Loeser, A.: Mammary Carcinoma: Response to Implantation of Male Hormone and Progesterone, Lancet **2**: 698, 1941. (*b*) Fels, E.: Treatment of Breast Cancer with Testosterone Propionate, J. Clin. Endocrinol. **4**: 121, 1944. (*c*) Boger, W. P.: Methyl Testosterone and Surgical Castration in the Treatment of Carcinoma of the Breast, ibid. **6**: 88, 1946. (*d*) Schwander, H., and Marvin, H.: Treatment of Carcinoma of the Human Breast with Testosterone Propionate: A Report of Five Cases, ibid. **7**: 423, 1947. (*e*) Farrar, J. H., and Woodard, H. G.: The Influence of Androgens and Estrogenic Substances on the Serum Calcium in Cases of Skeletal Metastases from Mammary Cancer, J. A. M. A. **118**: 339 (Jan. 31) 1942. (*f*) Adair, F.: The Use of the Male Sex Hormone in Women with Breast Cancer, Surg., Gynec. & Obst. **84**: 719, 1947. (*g*) Adair, F., and Herrman, J.: The Use of Testosterone Propionate in the Treatment of Advanced Carcinoma of the Breast, Ann. Surg. **123**: 1023, 1946. (*h*) Herrman, J., and Adair, F.: The Effect of Testosterone Propionate on Carcinoma of the Female Breast with Soft Tissue Metastases, J. Clin. Endocrinol. **6**: 769, 1946. (*i*) Herrman, J.; Adair, F., and Woodard, H. G.: The Use of Testosterone Propionate in the Treatment of Advanced Carcinoma of the Breast, Surgery **22**: 101, 1947. (*j*) Jones, H. W.: Testosterone in the Treatment of Advanced Breast Cancer; A Preliminary Report, South. M. J. **41**: 4, 1948. (*k*) Klass, Alan: Testosterone Propionate in the Treatment of Pulmonary Metastases from Breast Cancer; Report of a Case, Canad. M. A. J. **58**: 66, 1948. (*l*) Van Luin, J. J.: De behandling van mamma carcinoom metastases mit testosteron propionaat, Nederl. tijdschr. v. geneesk. **91**: 2834, 1947.
7. Thorn, G. W., and Engel, L. L.: The Effect of Sex Hormones on Renal Excretion of Electrolytes, J. Exper. Med. **68**: 299, 1938.
8. Kenyon, A. T.; Sandiford, I.; Byron, A. H.; Knowlton, K., and Koch, F. C.: The Effect of Testosterone Propionate on Nitrogen, Electrolyte, Water and Energy Metabolism in Eunuchoidism, Endocrinology **23**: 135, 1938.
9. Abels, J. C.; Young, N. F., and Taylor, H. C.: Effects of Testosterone Propionate on Protein Formation in Man, J. Clin. Endocrinol. **4**: 198, 1944.
10. Butler, A. M.; Talbot, N. B., and MacLachlan, E. A.: Effect of Testosterone Therapy on Concentration of Potassium in Serum, Proc. Soc. Exper. Biol. & Med. **51**: 378, 1942.

represent osteoblastic metastases, or, and most important, it may represent a combination of both processes existing simultaneously. Thus a rise in the level of alkaline phosphatase may mean more osteoblastic metastases rather than repair of osteolytic lesions. Adair and Herrman [6g] have reported one case with favorable response in which there was a rise in the level of alkaline phosphatase accompanying the calcification of the skeletal metastases. It must be borne in mind, however, that the level of the serum alkaline phosphatase is dependent on the degree of osteoblastic activity. Since it is well established that metastasis to bone without treatment may cause a rise in the level of serum alkaline phosphatase, it is our belief that this index is not a safe criterion of response to treatment.

Subjective changes which occur in patients receiving testosterone are well known. These include hoarseness, facial hirsutism and other signs of virilism; in addition, there is usually a decided increase in libido. This latter effect has been well described by Abel.[11] Enlargement of the clitoris and development of an acneform eruption on the trunk also occur and are usually very disturbing. Geist and his co-workers [12] have demonstrated that as a rule more than 200 mg. of testosterone propionate per month is required to produce masculinization and cessation of menses. These effects are lost slowly after treatment is discontinued. A sense of well-being and some relief of discomfort is common, but this effect is usually transient. In our cases, once the favorable systemic effect of testosterone was lost, another course of testosterone did not renew the initial effect; however, Herrman, Adair and Woodard [6i] have reported cases in which the response to a second course of testosterone duplicated the favorable response of the first.

REPORT OF CASES

Twenty consecutive patients were treated; 19 had carcinoma and 1 had lymphosarcoma. Twelve showed no significant improvement; 11 of these died within one year after the beginning of treatment, and 1 died after fourteen months. Six of the 12 patients had only soft tissue involvement; the other 6 had only skeletal metastases. It is interesting that 3 patients experienced skeletal metastases while under treatment. We have no evidence that the disease was accelerated in any of the 12 cases which did not respond. There were no unusual reactions to the treatment.

Four cases showed transient improvement. In 1, multiple cutaneous nodules on the thoracic wall showed decided regression; however, the systemic disease became progressively worse, and the patient died from cancer. In a second case, a fixed ulcerated mass in one breast became more movable, but the ulceration increased. There was a temporary gain in weight and a decided improvement in her general condition; the effect, however, was transient. The disease became more progressive, and cancer developed in the opposite breast. In a third case, with pleural involvement and a severe cough, a sense of well-being was established and the cough diminished. Shortly after testosterone therapy was omitted, the condition became worse and the disease progressed. The history of the fourth case is presented in detail.

Case 1.—C. C., a woman aged 66 years, was admitted in April 1944, complaining of a mass in the right breast. Examination disclosed the classic clinical signs of cancer. There was no evidence of metastasis. Because of the patient's general condition, the operation (April 12) was limited to a simple mastectomy. Microscopically, the lesion was carcinoma. The intramammary lymph nodes were involved. Roentgen therapy was given to the axilla. There was no evidence of disease until May 12, 1945, when a small lymph node developed in the right axilla. July 30, 1946, the node measured about 3 by 3 cm. Roentgenograms of the chest, lumbar part of the spine and pelvis showed no metastasis. The chemical content (calcium, phosphorus and alkaline phosphatase) and structure of the blood and the urine were normal. On June 30, 300 mg. of testosterone propionate ("oreton") was injected intramuscularly and 150 mg. twice weekly until a total of 3,750 mg. had been given. After six weeks the node was slightly smaller, and at the end of eleven weeks it was barely palpable. The patient gained 6 pounds (about 3 Kg.) and felt well. The usual signs of masculinization were present. On October 18, intramuscular administration of testosterone was omitted and oral adminstration of 30 mg. of testosterone daily was begun. After two weeks the dose was reduced to 10 mg. daily. Examination remained the same until July 3, 1947, when a node of 2 cm. was again palpable in the axilla. The amount of testosterone given orally was increased to 20 mg. daily. The node became progressively larger, and on September 11 a right axillary dissection was performed. No evidence of carcinoma was seen in the specimen. There was no evidence of disease at the last examination, on April 29, 1948.

Comment.—There was no question in our minds that, clinically the node palpated in the axilla before the start of testosterone therapy was characteristic of metastatic carcinoma. Unfortunately, no tissue was removed for microscopic examination, and it is possible that our impression was not correct. Therefore, in this case we cannot make any statement concerning the effects of testosterone therapy. However, we have another case, not included in this report, which is almost identical with the one previously described except that methyl testosterone was used and, when the axillary dissection was performed, the specimen did show carcinoma. That patient subsequently showed evidence of widespread metastases.

These 4 cases represent the borderline group in which it is difficult to evaluate the effects of the medication. The possibility that the temporary response was coincidental cannot be excluded. It is more likely, however, that testosterone did play some role in the regression of the disease. In each of these 4 cases the disease at the time of treatment was confined to soft tissue.

Four cases showed definite improvement: 1 with skeletal metastases, 1 with skeletal and soft tissue metastases and 2 with soft tissue involvement. The case histories follow.

Case 2.—J. C., a woman aged 42 years, was admitted on June 1, 1942, with a mass in the axillary portion of the left breast. Observations in roentgenograms of the chest were normal. On July 3 radical mastectomy was performed. The microscopic diagnosis was carcinoma. The axillary glands were not involved. There was no evidence of disease until April 26, 1946, when roentgenograms of the chest showed increased hilar adenopathy. Symptoms did not appear until October 25, when the patient began to complain of dyspnea and pain in the chest, pelvis and left leg. Roentgenograms of the chest showed pleural effusion on the right side. Examination of the thoracentesis fluid disclosed carcinoma cells. There was definite nodularity in the left supraclavicular space. Roentgenograms showed a large osteolytic lesion in the left iliac crest (fig. 1*A*) and a small lesion in the right femur. The chemical content (calcium, phosphorus and alkaline phosphatase) and structure of the blood and the urine were normal. On October 25, 30 mg. of testosterone propionate ("oreton") was injected intramuscularly, and 150 mg. was given twice weekly

11. Abel, S.: Androgenic Therapy in Malignant Disease of the Female Genitalia, Am. J. Obst. & Gynec. **49**: 327, 1945.
12. Geist, S. H.; Salmon, V. J.; Gaines, J. A., and Walter, R. S.: The Biologic Effects of Androgen (Testosterone Propionate) in Women, J. A. M. A. **114**: 1539 (April 20) 1940.

until a total dose of 4,050 mg. had been given. The dyspnea disappeared after two weeks. The fluid in the chest was almost completely absent according to roentgenologic studies on Jan. 1, 1947. On April 22 the osteolytic areas showed decided calcification and trabeculation (fig. 1 *B*). Except for the facial hirsutism, the patient was comfortable. Intramuscular administration of testosterone was discontinued on January 20 and oral administration of 30 mg. of testosterone daily was begun. The masculinization was maintained, and, after 900 mg. had been taken orally, the dose was reduced to 10 mg. daily on September 27. At that time the patient complained of headache and diffuse pain in the chest. Her condition became progressively worse; on November 3, dyspnea increased, she was losing weight and her general condition was deteriorating. Skeletal metastases became more widespread. Sixteen hundred cubic centimeters of fluid was aspirated from the chest. On November 3, 300 mg. of testosterone propionate ("oreton") was injected intramuscularly, and 150 mg. was injected twice weekly. This was continued for six weeks, but the patient's condition became progressively worse and she died on December 20.

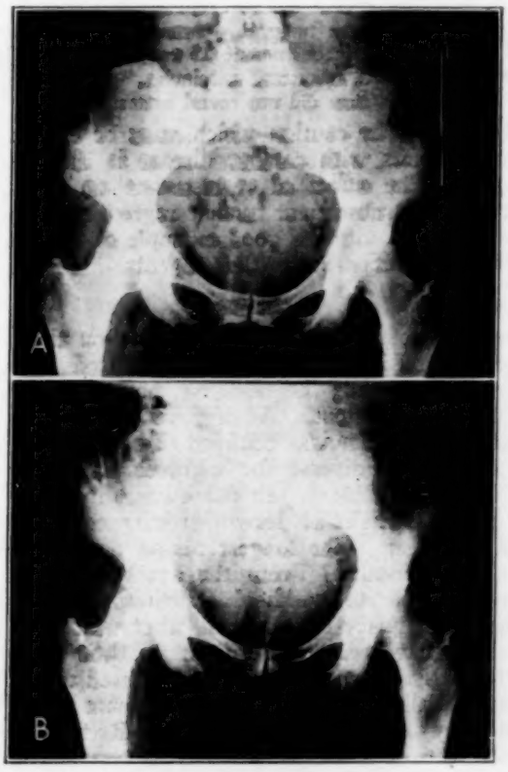

Fig. 1 (case 2).—*A*, before treatment. *B*, after treatment.

Comment.—This case illustrates that soft tissue and skeletal metastases may be affected favorably in the same patient. It is also noteworthy that a second course of testosterone had no effect on the progress of the disease. The testosterone therapy suppressed menstruation permanently. There were no menopausal symptoms. The improvement lasted for eleven months.

CASE 3.—J. O., a woman aged 58 years, was admitted on Sept. 17, 1946. She complained of a lesion on the scalp of five months' duration. A report of biopsy was "suggestive of malignant growth." There was a raised red scaly lesion, 5 by 5 cm., on the left side of the scalp (fig. 2 *A*). There was no hair in this area. The lesion was believed to be metastatic. With great hesitancy, the patient finally admitted that she had known of a lump in the left breast for several years and consented to an examination. In the left breast there was a large ulcerated lesion, with induration of the entire breast, and multiple cutaneous nodules extending into the left axilla. The right axilla contained a firm node 2 by 2 cm. Multiple small subcutaneous nodules extended onto the abdomen. In addition, there was a hard mass, suggestive of intraperitoneal metastases, in the right lower abdominal quadrant. Roentgenograms of the chest and lumbar part of the spine showed no evidence of metastasis. Biopsies from the scalp and thoracic wall showed carcinoma. Sept. 19, 1946 the blood chemistry and morphology as well as the urine were normal. On September 18, 300 mg. of testosterone propionate ("oreton") was injected intramuscularly and 150 mg. twice weekly, until 4,650 mg. had been given. During the first two weeks the patient complained of abdominal cramps and nausea. There was a decided response. The scalp lesion healed, and hair grew in the area (fig. 2 *B*). The lesion of the breast regressed, and many of the metastatic nodules resolved. The patient gained 13 pounds (about 6 Kg.). There was no significant change in the chemical content of the blood. On December 30, intramuscular administration of testosterone was discontinued and oral administration of 30 mg. of testosterone daily was begun. The masculinization persisted, and the patient felt well. All the lesions continued to regress. On Feb. 21, 1947, the amount of orally administered testosterone was reduced to 20 mg. daily. Masculinization was still present. On March 4 the patient began to complain of pain in the back. Roentgenograms showed metastases to the skull, lumbar vertebrae and lungs. Testosterone therapy was discontinued, and 7.5 mg. of diethylstilbestrol monomethyl ether ("monomesterol") daily was given. The pain in the back did not improve; treatment with diethylstilbestrol monomethyl ether was stopped, and on May 12 roentgen rays were given to the lumbar part of the spine, with complete relief of pain. The patient continued to feel well for approximately five to six months, despite multiple metastases; however, her condition became progressively worse, and metastases to the liver and other organs developed. She died on June 7, 1948, twenty-one months after the beginning of hormone therapy.

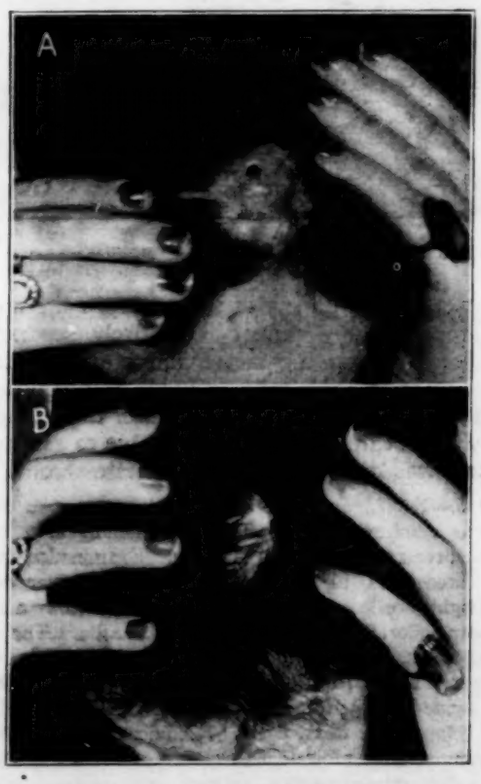

Fig. 2 (case 3).—*A*, before treatment. *B*, after treatment.

Comment.—The healing of the scalp metastases and regression of the cutaneous nodules represent definite evidence of the effect of testosterone on the soft tissue metastases. Interesting microscopic changes in the

composition of the tumor in a series of biopsies were seen. Skeletal metastases developed in this patient while she was receiving masculinizing doses of testosterone. The use of large doses of estrogenic substances did not alter the course of the disease.

CASE 4.—C. V., a woman aged 43 years, was admitted June 3, 1947. In August 1944 a left radical mastectomy was performed for cancer followed by postoperative radiation. The patient was well until March 1947, when she began to complain of pain in the pelvis. Roentgenograms showed complete destruction of the inferior ramus of the left pubis and ischium; there were also destructive lesions in the right femur and right humerus (fig. 3 *A*). Between March 15 and April 16, small doses of roentgen rays had been given to the pelvis, lumbar part of the spine and right shoulder at another hospital, without relief. There was no external evidence of disease except a slight limp. On June 17 she received 300 mg. of testosterone propionate ("oreton") intramuscularly and 150 mg. twice weekly thereafter, up to a total dose of 3,850 mg. This was followed by oral administration of a maintenance dose of 60 mg. of testosterone daily. After two months, the bone lesions began to calcify and there was complete absence of pain (fig. 3 *B*). This palliation continued until April 1948, when again the patient complained of pain in the shoulder and pelvis. Roentgenograms showed increase in the osteolytic metastases. Another course of testosterone was begun, but the disease continued to progress.

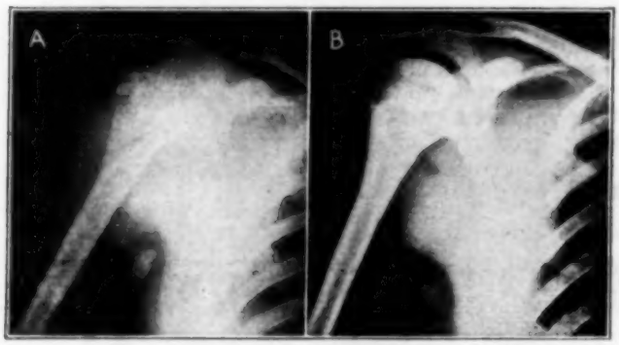

Fig. 3 (case 4).—*A*, before treatment. *B*, after treatment.

Comment.—The effects of the roentgen therapy and testosterone therapy cannot be entirely separated in this case; however, the fact that the patient did not receive any appreciable relief from the roentgen therapy, but did show decided improvement after the testosterone therapy was begun, makes it reasonable to assume that the effect was due primarily to the testosterone.

CASE 5.—N. T., an obese diabetic Negro woman aged 62 years was admitted Dec. 10, 1946, complaining of a mass in the right breast of two years' duration. Examination disclosed a hard fixed mass, 10 by 7 cm., in the upper outer quadrant of the right breast. There was definite cutaneous adherence and linear induration extending into the axilla. The size of the mass and its position prevented the arm from coming against the thoracic wall. Roentgenograms of the chest, lumbar part of the spine and pelvis did not reveal metastasis. Decided cardiac enlargement was evident. A clinical diagnosis of cancer was made, and a radical mastectomy advised. The patient categorically refused major surgical procedures. A biopsy showed carcinoma. On December 17, 300 mg. of testosterone propionate ("oreton") was injected intramuscularly and 150 mg. twice weekly, until 2,250 mg. had been given. On Jan. 2, 1947, after administration of only 900 mg. of testosterone, there was definite regression of the breast tumor and the patient stated that she was again able to put her arm by her side. At this time she complained of weakness, and there was increased swelling of the ankles. These symptoms were attributed to increasing cardiac decompensation resulting from water retention; however, testosterone therapy was continued. On February 15 the mass showed further regression and the linear extension into the axilla was no longer palpable. Because of the cardiac problem, testosterone therapy was discontinued and the residual mass was treated with radiation. Telecurietherapy was administered to the residual tumor between February 17 and March 23. The tumor continued to regress, and by December 29 it had disappeared; there was, however, a firm lymph node in the right axilla. The patient did not return again until Feb. 24, 1948, at which time the tumor had recurred, forming a mass 7 by 7 cm., with a cutaneous nodule 0.5 cm. in diameter. Biopsy of this nodule showed metastatic carcinoma. A roentgenogram of the chest at this time did not reveal metastasis.

Comment.—The caution which must be exercised in treating patients with cardiac disease is illustrated in this case. The effect of testosterone on the breast tumor and the subsequent further regression with telecurietherapy constitute a good example of the response of soft tissue metastases to these agents.

COMMENT

The favorable effects of testosterone on the course of the disease in some cases of advanced mammary cancer are reported; the response, however, is unpredictable and transient. Adair [6f] reported 3 patients, in whom the disease was confined to bone, living without evidence of disease for eighteen to twenty-four months after treatment. In our 4 cases in which definite improvement was shown, recurrence developed within one year. The longest period of improvement was eleven months. From the available evidence it seems advisable to withhold testosterone therapy in advanced mammary cancer until other well established procedures have reached the limits of their usefulness. It is for this reason that we have not used testosterone prophylactically as practiced by Prudente [3] and more recently by Adair [5] and Snapper.[4] Because several patients who obtained palliation from testosterone suffered a recurrence of the disease after treatment was stopped, it is suggested that treatment should continue until the palliative effect is no longer evident.

It must be remembered that surgical castration and roentgen sterilization frequently produce results which are comparable to those seen with testosterone therapy and these procedures should not be abandoned. It is true that the availability of a constitutional agent such as testosterone is a great comfort to both patient and physician; however, final evaluation is not possible until further and more prolonged studies have been conducted. At present, the Therapeutic Trials Committee of the Council on Pharmacy and Chemistry of the American Medical Association is conducting an extensive and coordinated study of testosterone therapy in advanced mammary cancer, which is being pursued by various groups throughout the country. It is hoped that this study will produce a significant number of cases, with treatment under controlled conditions, to permit more definite conclusions.

SUMMARY AND CONCLUSIONS

Twenty patients with advanced mammary cancer were treated with testosterone propionate ("oreton"). Twelve showed no significant improvement, and 11 of these died within one year after the beginning of the treatment. One patient with lymphosarcoma of the breast was not improved. Four patients showed transient improvement of short duration. The palliative effects of testosterone were striking in four cases, but the duration of response was limited. No evidence that testosterone therapy can cure advanced breast cancer was observed, and palliative results can be anticipated in only a relatively small number of patients.

PENICILLIN IN TETANUS

A Clinical Analysis of Fifty-Nine Cases

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The clinical picture of generalized tetanus has been known for thousands of years; its causative agent was discovered over sixty years ago; almost perfect methods of prophylaxis are known and being practiced, and yet the disease remains as one of the most dangerous infectious complications of wounds, because of the inadequate methods of treatment.

The studies of Abel and his co-workers [1] and Firor and his co-workers [2] have demonstrated that the value of tetanus antitoxin is limited once the symptoms of the disease are well established, and when an overwhelming amount of toxin is fixed by the cells of the central nervous system the invariable outcome is death.

Even if the outcome of generalized tetanus is always grave, there are patients that respond favorably to the limited but well known therapeutic measures. This is especially true among patients for whom treatment is started before the onset of the serious manifestations of the disease. In spite of early treatment and, at times, heroic measures, the mortality rate of the disease is still too high.

Although judgment of the outcome in tetanus is not always exact, it is known that a short incubation period, the rapid appearance of muscle spasms after onset, frequent and severe convulsions and a poor response to sedation are always signs of a poor prognosis. In these cases the physician is almost at a loss from the start.

In view of the inadequate therapeutic measures available for the management of the disease, the favorable reports on the use of penicillin [3] and the demonstration that it is an antibiotic for Clostridium tetani in vivo,[4] we were prompted to give it a fair trial in a large group of cases.

MATERIAL AND METHODS

During a period of twenty months, between July 1945 and March 1947, there were 2,364 medical admissions to the San Juan City Hospital. Fifty-nine (2.4 per cent) of the patients were suffering from tetanus. There were 38 white patients, of whom 26 were male and 12 female, and 21 were Negro, 13 being male and 8 female. The youngest was 8 years old and the oldest 70, with an average age of 22.7 years. There were 2 under 10, 25 under 20, 37 under 30, 49 under 40, 53 under 50, 58 under 60, and 1 was 70 years old.

The incubation period was known in 51 cases, varying between two days and three months. There were 15 with an incubation period between one and five days, 20 between six and ten days, 8 between eleven and fifteen days, 2 between sixteen and twenty days and 6 over twenty-one days. The average incubation period for the whole group was eight and four-tenths days and for the cases with fatal outcome five and seven-tenths days.

The portal of entry was discovered in 57 instances: the feet in 24, the leg in 8, the hand in 7, the arm in 7, the mouth in 2, the anus in 2, the uterus in 2, the abdominal wall in 2 and the penis, thigh and cheek in 1 instance each.

The nature of the lesion was evident in 54 cases. Puncture wounds due to rusty nails, splinters of wood, broken glass, tin cans and rusty wire were noticed in 17 cases. Chiggers were responsible for infection in 7 cases, lacerations in 5, abrasions in 5, ulcerations in 4, incised wounds in 3, abortions in 2 and hypodermic injections in 2 (a liver injection in the arm and an injection of fibrinogen in the abdominal wall). In 2 instances anal fissures were discovered and thought to be the portals of entry in the absence of any other open lesion. In another, a carious tooth was picked with a blunt instrument and in a few days the disease developed. Extraction of a tooth, an abscess of the cheek, a burn, a contusion, a human bite and a surgical wound for a herniotomy were each responsible for a case.

TABLE 1.—*Observations on Admission*

Observations	Number of Cases	Percentage
Stiffness of the jaw	59	100
Trismus	59	100
Dysphagia	54	91
Rigidity of the neck	52	88
Abdominal rigidity	52	88
Restlessness	49	83
Back pain	48	81
Hyperactive reflexes	44	74
Spasticity of the limbs	35	60
Fever	34	58
Stiffness of the limbs	32	54
Convulsions	29	49
Opisthotonos	29	49
Leukocytosis	21	35
Oppression of the chest	21	35
Headache	13	22

The disease in 56 of the cases was classified as generalized tetanus and in 3 as cephalic tetanus. No cases of the local disease were observed. Twenty-nine patients had convulsions before admission; this symptom developed in 12 after hospitalization (in 5 within the first twenty-four hours, 6 within forty-eight hours and 1 within seventy-two hours after admission), while 18 never suffered from this symptom.

The time between the onset of symptoms and the occurrence of convulsions or muscle spasms was known in 35 cases—in 10 within the first day, in 6 within two days, in 3 within three days, in 3 within four days, in 12 within five days, in 1 within six days, in 2 within seven days, in 2 within eight days, in 3 within nine days and in 1 each within thirteen, sixteen and twenty days. Two of the 12 patients in whom convulsions developed after admission died from the disease.

The most frequent clinical observations on admission were stiffness of the jaw, trismus, dysphagia, rigidity of the neck, abdominal rigidity, restlessness, back pain,

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4. Weinstein, L., and Wesselhoeft, C.: Penicillin in Treatment of Tetanus: Report of Two Cases, New England J. Med. **233**: 681-684, 1946.

hyperactive reflexes, spasticity of the limbs, fever, stiffness of the limbs, opisthotonos, convulsions, oppression of the chest and headache. Leukocytosis was present in 35 per cent of the cases (table 1).

On admission every patient received 100,000 units of antitetanic serum intravenously after a negative reaction to a dermal test for sensitivity. In the great majority of the cases 100,000 units was given intramuscularly as well. The portal of entry, when accessible, was debrided and excised when necessary, after the infiltration of the surrounding tissues with 20,000 units of antiserum. The lesion was left open and treated locally with hydrogen peroxide compresses. Daily intramuscular injections of 5,000 to 10,000 units of antiserum were given for the next three days. Forty-two patients received more than 250,000 units of the antiserum. Two thousand to 4,000 cc. of 5 per cent dextrose in isotonic sodium chloride solution was given intravenously in accordance with the patients' needs for hydration, and an indwelling stomach tube was left in situ for the nutrition of the most seriously ill patients. Phenobarbital sodium was given hypodermically in doses of 2 grains (0.13 Gm.) or more every two to three hours for the control of convulsions. In some cases we had to resort to a mixture of ether and oil given by rectum to relieve the painful convulsions. Treatment with penicillin, in doses of 15,000 to 20,000 units intramuscularly every three hours, was started on admission, and the total unitage of the drug was not limited.

TABLE 2.—*Analysis of Deaths*

Sex	Race	Age, Yr.	Lesion	Organ	Incubation, Days	Amount of Medication: Tetanus Antitoxin	Amount of Medication: Penicillin	Hospital Stay
M	N	19	Ulcer	Penis	6	200,000 u.	40,000 u.	7 hr.
M	N	44	?	?	?	200,000 u.	45,000 u.	10 hr.
F	W	54	Chiggers	Foot	4	315,000 u.	600,000 u.	6 days
F	W	22	Caries	Molar	5	200,000 u.	140,000 u.	21 hr.
M	W	18	Laceration	Arm	3	250,000 u.	1,560,000 u.	11 days
F	W	70	Puncture wound	Foot	13	270,000 u.	1,320,000 u.	9 days
F	N	28	Ulcer	Leg	?	260,000 u.	600,000 u.	6 days
M	W	55	Abscess	Cheek	4	350,000 u.	400,000 u.	3 days
F	W	16	Abortion	Uterus	7	245,000 u.	930,000 u.	8 days
M	N	22	Incised wound	Hand	5	180,000 u.	1,460,000 u.	5 days
F	W	39	Hypodermic	Arm	3	250,000 u.	100,000 u.	36 hr.
M	N	10	Puncture wound	Foot	7	300,000 u.	2,200,000 u.	15 days
Average....		35			5.7	251,666 u.	796,000 u.	5.5 days

RESULTS

There were 12 patients who died and 47 who recovered, with a gross mortality rate of 20.3 per cent. The average hospital stay for the whole group was nineteen days and for the patients that died five and five-tenths days. The average length of life after the onset of symptoms in the cases in which the disease was fatal was eleven and six-tenths days. Four lived for seven, ten, twenty-one and thirty-six hours, respectively, after admission. These did not receive the full benefit of treatment. Only 8, therefore, could be considered as hospital deaths, the hospital mortality rate being 13.5 per cent. The 59 patients received an average total of 1,800,000 units of penicillin, while the 12 that died received an average of 796,000 units. It is known that the clinical improvement in most established infections usually occurs within eighteen to seventy-two hours after the beginning of treatment with penicillin. Granting that the drug was beneficial, 8 patients were given full chance for improvement or recovery, 2 a partial chance and 2 were not given enough drug to benefit them at all. The mortality rate in spite of efficient penicillin therapy was, therefore, 17.6 per cent (10 deaths) (table 2). If the total unitage of the drug were considered as essential in the control and cure of the infection, perhaps the relatively small amounts given to 4 of the patients would explain the fatal outcome, but other factors may have been responsible, since much heavier doses failed to save the life of the other 8. The average amount of tetanus antitoxin administered to the 59 patients was 260,000 units, while the patients in whom the disease terminated fatally received 251,666 units. The difference was so slight that the amount of antitoxin had little to do in the issue of life or death. It was evident that as an adjuvant penicillin produced beneficial effects, as demonstrated by the low mortality rate. Obvious benefit from the drug was recorded among 11 patients with bronchopneumonia complicating tetanus. Seven of these recovered, and 4 died.

The duration and frequency of the convulsions were not benefited by either penicillin or tetanus antitoxin. Two of the patients who died had received large doses of antitoxin before the onset of convulsions, and in both the disease was classified as mild. It is evident that in these 2 patients the outcome could not be determined on admission.

Among the 26 white male patients in this series only 2 died, yielding the surprisingly low mortality rate of 7.6 per cent, while of the 13 Negro male patients 30.8 per cent died. Of the 12 white female patients 5 died, with a mortality rate of 41.7 per cent, while of the 8 Negro female patients 1 died, with a mortality rate of 12.5 per cent. Thus, the mortality rate among the white persons was 15.4 per cent and among the Negroes, 30.0 per cent (table 3). This difference in the mortality rate in the two races is unexplained, since there was no gross difference in the incubation period, nature of the lesions and portal of entry in the two groups. By the same token, the difference in the mortality rate of male patients as compared with that of female patients lacks an explanation.

From the data presented in this paper it appears that tetanus is a more serious illness among patients older than 50 and younger than 10, as evidenced by a 50 per cent mortality rate among those older than 50 and younger than 10, as compared with 15.5 per cent among those between 11 and 50 years of age, but there were only 2 patients younger than 10 and 6 older than 50. Perhaps a larger series would have yielded different results (table 5).

TABLE 3.—*Mortality Rate: Sex and Race*

	Male	No. of Deaths	Percentage	Female	No. of Deaths	Percentage
White.....	26	2	7.6	12	5	41.7
Negro.....	13	4	30.8	8	1	12.5
Total.....	39	6	15.4	20	6	30.0

Six deaths (40 per cent) were recorded among the 15 patients with an incubation period of five days or less, 3 (15 per cent) of the 20 with an incubation of six to ten days and only 1 (12.5 per cent) among those with an incubation period of more than ten days. Two of the patients with no known periods of incubation died from the disease, but the rapid clinical course in these

2 suggests that it was relatively short (table 4). Among the 10 patients in whom convulsions appeared within twenty-four hours after onset of the disease, 6 (60 per cent) died; within the first forty-eight hours 3 (50 per cent) died, and within seventy-two hours 2 (33.3 per cent died. Information was not obtained in the other 3 fatal cases. These observations substantiate the relationship of a high mortality rate with a short incubation period and a rapid onset of convulsions (table 6).

TABLE 4.—*Incubation Period and Mortality Rate*

	Incubation Period				Mortality Rate	
Number of days	1-5	6-10	11-15	16-20	Over 21	Total
Number of cases	15	20	8	2	6	51
Number of deaths	6	3	1	..	..	10
Mortality	40%	15%	12.5%	0%	0%	19.6%

The mortality rate among those patients with a portal of entry in the lower extremity was 13.3 per cent, of those in upper extremities 29 per cent, in the trunk 26.6 per cent and in the head 66.6 per cent. No portal of entry was discovered in 1 fatal case. Survival from postabortion tetanus is rare. One of our patients was treated with vaginal douches of hydrogen peroxide, with improvement, but the value of this procedure is questionable. In our second case oxygen was bubbled into the uterus, but this was to no avail (table 7).

TABLE 6.—*Time Between Onset of the Disease and the Appearance of Convulsions; Mortality Rate*

Day	Number of Cases	Number of Deaths	Mortality Rate, Percentage
First	10	6	60
Second	6	3	50
Third	3	1	33.3
Fourth	3	..	..
Fifth	2	..	..
Sixth	1	..	..
Seventh	2	..	..
Eighth	2	..	..
Ninth	3	..	..
Thirteenth	1	..	..
Sixteenth	1	..	..
Twentieth	1	..	..
Total	35	10	28.5

Puncture wounds yielded a mortality rate of 11.8 per cent, chiggers 14.3 per cent, lacerations 20 per cent, abrasions 0 per cent, ulcerations 50 per cent, incised wounds 33.3 per cent, endometritis 50 per cent and hypodermic injections 50 per cent. As a rule the lesion looked inoffensive, and it appears that for that reason none of our patients received prophylactic inoculations after injury (table 8).

The actual cause of death was known in the 12 fatal cases. In 7, it was due to respiratory paralysis and overwhelming toxemia, in 4 to complicating bronchopneumonia and in 1 to extreme dehydration. Severe serum sickness contributed to 1 death. Milder reactions to antitetanic serum were seen in 4 patients who recovered. No causative agent was demonstrable in the cases of bronchopneumonia, but we suspect that in the fatal cases either the causative agent was penicillin resistant, the drug was not administered in large enough doses to effect a cure or these may have been instances of severe aspiration pneumonia.

COMMENT

The potential value of penicillin in the treatment of tetanus has been explored by various investigators, and the results have been controversial. An exact evaluation of the usefulness of the drug is at present impossible, since few planned clinical studies have been made and the great majority of reports in the literature are based on small groups of cases.

A clinical study of 59 cases of tetanus is hereby presented, in which certain conclusions are justified. All the patients received large amounts of penicillin and antitetanic serum and were benefited by other well known therapeutic measures in the accepted treatment of the disease. There were patients of almost all ages, and there was a fair sampling as to sex and race. It being a planned study, precautions were taken that all patients were handled as similarly as possible and that the most exact information was obtained. Twelve patients died, yielding a gross mortality rate of 20.3 per cent. Of these, only 10 received adequate amounts of penicillin to guarantee full benefit, with a mortality rate of 17.6 per cent. Such a low mortality rate among a large group of cases of tetanus is difficult to explain, when in the best of institutions the mortality rate may be as high as 50 to 60 per cent. It may be suggested that Puerto Ricans are naturally resistant to the disease.

TABLE 5.—*Mortality Rate: Age Groups and Sex*

	Number of Patients Aged 1-10	Deaths	Number of Patients Aged 11-20	Deaths	Number of Patients Aged 21-30	Deaths	Number of Patients Aged 31-40	Deaths	Number of Patients Aged 41-50	Deaths	Number of Patients Aged 51-60	Deaths	Number of Patients Aged 61-70	Deaths
Male white	1	..	12	1	3	..	8	..	..	..	2	1	..	..
Female white	..	..	3	1	4	1	3	1	..	..	1	1	1	1
Male Negro	1	1	8	1	2	1	..	..	2	1	..	..	..	..
Female Negro	..	..	..	..	3	1	1	..	2	..	2	..	..	..
Total	2	50%	23	13%	12	25%	12	8.3%	4	25%	5	40%	1	100%

TABLE 7.—*Portal of Entry; Mortality Rate*

Portal of Entry	Number of Cases	Number of Deaths	Percentage of Deaths
Foot	24	3	12.5
Leg	8	1	12.5
Arm	7	1	14.3
Hand	7	2	28.6
Mouth	2	1	50.0
Anus	2	0	00.0
Uterus	2	1	50.0
Abdomen	2	0	00.0
Penis	1	1	100.0
Thigh	1	0	00.0
Cheek	1	1	100.0
Total	57	11	19.5

That this is not true has been demonstrated by Francisco,[5] who reported a mortality rate of 58.1 per cent in a large group of natives of Puerto Rico receiving tetanus antitoxin as the only form of treatment for tetanus.

5. Francisco, R.: A Clinical and Epidemiological Study of Tetanus in Puerto Rico: A Study of One Hundred Cases Seen at the Arecibo District Charity Hospital in a 2½ Year Period, Clinics 3: 373-414, 1944.

There is abundant experimental proof to deny any favorable effects of large amounts of antitoxin in severe well established generalized tetanus. An analysis of our data shows that tetanus antitoxin not only is useless in relieving the convulsions but also failed to prevent the symptom in 12 of the patients hospitalized early in the course of the disease. On admission, these patients appeared only moderately ill, and the disease was labeled as mild tetanus. It seems that some time elapsed between the fixation of the toxin by the cells of the central nervous system and its diffusion to the neuromuscular end organ and that the quantity of toxin released was large enough to produce symptoms of such severity as to cause the death of 2 of these patients. This tends to demonstrate that judgment as to the outcome of tetanus is inexact when based on the presence or absence of convulsions and that in some cases the issue of life or death is not affected by the administration of antitoxin, no matter what the quantity or how early in the course of the disease it is given. It is emphasized that the mortality rate among the 12 patients in whom convulsions developed after hospitalization (16.6 per cent) approached that for the whole group (20.3 per cent).

TABLE 8.—*Nature of Lesion; Mortality Rate*

Type or Cause of Lesion	Number of Cases	Number of Deaths	Mortality, Percentage
Puncture	17	2 (feet)	11.8
Chiggers	7	1 (feet)	14.3
Lacerations	5	1 (arm)	20.0
Abrasions	5	..	00.0
Ulcerations	4	2 (leg)(penis)	50.0
Incised wound	3	1 (hand)	33.3
Abortions	2	1	50.0
Hypodermic injection	2	1 (liver, arm)	50.0
Anal fissures	2	..	00.0
Carious tooth	1	1	100.0
Tooth extraction	1	..	00.0
Abscess	1	1 (cheek)	100.0
Burn	1	..	00.0
Contusion	1	..	....
Human bite	1	..	....
Surgical wound	1	..	....
Total	54	11	18.3

It appears that penicillin is useless in the prevention of the diffusion of the tetanus toxin through the tissues or its fixation by the nerve cells. By the same token, it does not relieve or prevent convulsions in already established tetanus.[6] However, the favorable results obtained in this series of cases indicate that it is a valuable adjuvant in the treatment of the disease in combination with the other accepted measures. Penicillin has been shown to be an antibiotic for Clostridium tetani in vitro, and this property of the drug has been confirmed in vivo by Weinstein and Wesselhoeft,[4] who noted the disappearance of the tetanus bacilli from the wounds of 2 patients twenty-four hours after the administration of the drug.

Perhaps the low mortality rate reported in this paper could be explained by this property of the drug, which by paralyzing the multiplication of Clostridium tetani reduced or prevented further production of toxin. The maintenance of a proper blood level of the drug may have been beneficial in preventing secondary bacterial infections. That it was efficient in curing bacterial complications incident to the disease is evidenced by the recovery of 7 of our 11 patients suffering from bronchopneumonia. The failure of treatment with the drug in the fatal cases may have been due to a penicillin-resistant strain of bacteria, to small doses of the drug or to instances of aspiration pneumonia.

Definite conclusions as to the value of penicillin in tetanus must await more extensive studies in larger groups of cases. To deny its value on the basis of a high mortality rate among a small number of cases would perhaps be harmful, especially when the majority of the patients who died had not received the full benefit of the drug.[7]

It should be reemphasized that the most accurate prognostic signs of the disease are the length of the incubation period and the rapidity of appearance of muscle spasms after the onset of the disease and that, in spite of the favorable results reported in this paper, penicillin would be useless in the treatment of the disease if not used in conjunction with supportive measures for the maintenance of proper hydration and electrolytic balance, good nutrition, efficient sedation, neutralization of the free toxin with tetanus antiserum and proper debridement of the portals of entry if accessible.

SUMMARY AND CONCLUSIONS

On the basis of our observations of 59 patients with tetanus, we conclude that penicillin is a useful adjuvant in the treatment of the disease. The gross mortality rate was 20.3 per cent, the mortality rate among those patients that received a fair trial with penicillin being 17.6 per cent.

The favorable action of the drug may be attributed to its antibiotic property against the tetanus bacillus, that, by hindering its growth and multiplication, eliminated or paralyzed the production of the toxin.

Penicillin may also act as an antibiotic for other bacteria, preventing or curing already established complications, such as bronchopneumonia.

Penicillin is considered useless in the prevention of convulsions and in the elimination of the free toxin in the body or the already fixed toxin in the cells of the central nervous system.

The administration of large amounts of antitoxin is recommended to neutralize the toxin that is free in the body or being produced by Clostridium tetani.

The antitoxin is useless in preventing the onset of or in eliminating the convulsions of tetanus when present.

It appears from the analysis of the data of 12 of our patients that some time elapses between the fixation of the tetanus toxin by the nerve cells and its diffusion to the tissues resulting in convulsions.

The presence of convulsions in tetanus is not a measure of its severity, and the formulation of a good prognosis in the absence of this symptom may be erroneous.

Debridement of infected wounds, maintenance of proper hydration and electrolyte balance, good nutrition and sedation are considered as important as the administration of antitoxin or penicillin in the treatment of tetanus.

It is reemphasized that the mortality rate in tetanus is higher in the cases with short incubation period and rapid onset of convulsions.

The early recognition of the disease and the rapid institution of treatment with all available measures may have been contributory to the low mortality rate reported in this paper.

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6. Neter, E.: Effects of Penicillin, Claracin and Streptomycin upon Tetanus Toxin, J. Infect. Dis. **76**: 20-23, 1945.

7. Altemeier, W. A.: Penicillin in Tetanus, J. A. M. A. **130**: 67-72 (Jan. 12) 1946.

Special Article

CARCINOMA OF THE BREAST

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New York

This article is the fifteenth of a series to be published by the American Medical Association in cooperation with the American Cancer Society. The series is designed to aid in the early diagnosis of cancer and thereby to gain more effective results in treatment.

Cancer of the breast is one of the great diseases with which physicians have struggled since time immemorial. For the modern physician, however, cancer of the breast is a greater challenge than it was to his colleagues of even a generation ago, because today there are improved diagnostic methods that often make it possible to recognize the disease while it is still early, and there are new therapeutic methods that give better control over it. Unfortunately, this new knowledge has not as yet been fully digested and applied. There is a long way to go in the education of both the medical profession and the public. In a recent series of cases coming to the

ORDER OF INCIDENCE	SITE	SEX	ANNUAL INCIDENCE
1	BREAST	FEMALE	80.0
2	CERVIX UTERI	FEMALE	34.3
3	SKIN	MALE	29.2
4	STOMACH	MALE	27.1
5	COLON	FEMALE	24.4
6	PROSTATE	MALE	23.2
7	SKIN	FEMALE	19.8
8	COLON	MALE	19.6
9	STOMACH	FEMALE	17.6
10	RECTUM & RECTOSIGMOID	MALE	15.2
11	LUNG	MALE	14.7
12	OVARY	FEMALE	12.2
13	RECTUM & RECTOSIGMOID	FEMALE	12.1
14	FUNDUS UTERI	FEMALE	11.9
15	BLADDER	MALE	11.5
16	LIP	MALE	6.8
17	LEUKEMIA	MALE	6.3
18	PANCREAS	MALE	5.7
19	LIVER	FEMALE	5.5
20	BLADDER	FEMALE	5.2

ALL SITES FEMALE - 270.8 ALL SITES MALE - 231.8

Fig. 1.—Annual incidence of cancer per hundred thousand population, New York state exclusive of New York City, 1942, 1943 and 1944.

Presbyterian Hospital in which a careful study of the manner of diagnosis was made, it was found that wrong medical advice had been given to 27 per cent of the patients by the first physician whom they consulted. Surely here is an opportunity for better education of physicians.

The patients themselves must, of course, bear a measure of responsibility for delay. Many women delay consulting a physician for a long time after they discover that they have a tumor of the breast: ignorance, negligence and fear all play a part in this delay.

I believe that women should be educated in college hygiene courses, and by every other available method of propaganda, to examine their own breasts once a month, in the middle of the menstrual cycle when mammary engorgement is at a minimum. They should be taught to consult a physician promptly whenever they feel a lump or whenever discharge from the nipple or any asymmetry of the breast is discovered.

From the Department of Surgery and the Laboratory of Surgical Pathology of the School of Medicine of Columbia University.

THE PROBLEM OF DIAGNOSIS

FREQUENCY OF CANCER OF THE BREAST

The first step toward better diagnosis of cancer of the breast is a full realization of its frequency. According to Levin's [1] recent morbidity data for New York state the breast is by far the most frequent site for cancer in either sex (fig. 1). In women it is almost

Fig. 2.—Palpation of the supraclavicular regions.

twice as frequent as any other type of cancer. About 4 per cent of all adult women contract the disease. It is rare before the age of 25, but from then on its incidence increases throughout the whole life span.

These facts should produce in the mind of every physician an alert suspicion of the presence of cancer of the breast whenever anything abnormal is seen or felt in the course of examination of the breasts. Their examination is an important part of every physical examination. The value of careful routine examination of the breasts has been well established in our clinic, where 3.4 per cent of the total number of cancers of the

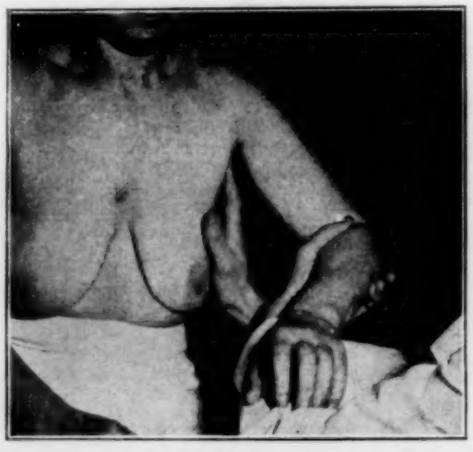

Fig. 3.—Palpation of the axilla.

breast were detected by such routine examination of patients who came to consult regarding some wholly irrelevant symptom.

EXAMINATION OF THE BREAST

A good deal of the success with which early cancer of the breast is detected depends on the care taken in

1. Levin, M. L.: Cancer Morbidity in New York State, personal communication to the author.

the examination of the breasts. The examiner must study the breasts as a separate step in his complete physical examination. If he merely passes his hand over his patient's breasts while she sits erect, as he prepares to examine her heart and lungs, he will often miss lesions of the breasts. An adequate examination

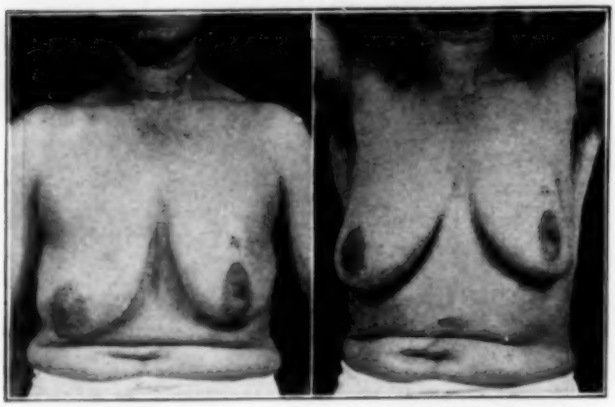

Fig. 4.—Inspection of the breasts with the arms at the sides and with the arms raised.

is a well ordered procedure including several different steps and requiring ten or fifteen minutes even when no abnormality is found. When the examiner finds something that arouses his suspicion that the breast may be diseased still other maneuvers are required.

I have found it advantageous to develop .. routine for examining the breasts because following an orderly routine guards against overlooking important details.

The procedure begins with examination of the supraclavicular and axillary regions. The patient sits on the table facing the examiner, with her legs over its side. The supraclavicular regions are conveniently palpated as the examiner stands behind the patient (fig. 2). In the examination of the axilla (fig. 3) it is essential that the pectoral muscles be relaxed. To achieve this the examiner supports the patient's arm on one of his

Fig. 5.—Palpation of the breast. The patient lies supine with a small pillow under her shoulder on the side being examined.

own. He then palpates with the tips of the fingers of his other hand. The more gentle his palpation the better he will feel lymph nodes lying against the thoracic wall. Lymph nodes high up in the axilla are difficult or impossible to feel. In obese patients palpation of the axilla is particularly unreliable.

Not only the number, but the consistence and movability of the axillary lymph nodes should be noted. They may be fixed to the underlying chest wall or the overlying skin. My colleagues and I have found it useful to attempt to measure the size of the largest axillary node, estimating transverse diameter in centimeters.

Palpation is unfortunately very inaccurate in determining whether axillary lymph nodes contain metastases. In the Presbyterian Hospital series of cases in which the examiner thought these nodes not to be involved 44 per cent were found by microscopic examination to contain metastases. On the other hand, in the cases in which the examiner made a clinical diagnosis of axillary metastases, 15 per cent of the patients proved not to have them.

The next step in our routine is a critical inspection of the breasts themselves, first with the patient's arms at her sides and then with the arms raised high above her head (fig. 4). The examination must be conducted in a good light, for nuances of light and shade and slight changes in contour of the breasts are of great importance and may be missed if the lighting is poor. The examiner compares the contour of the two breasts,

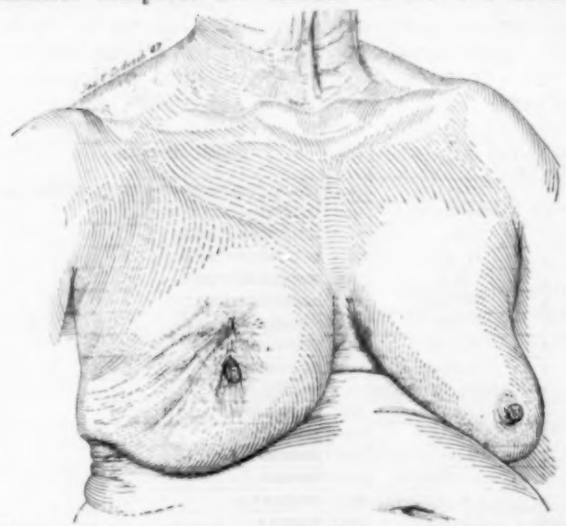

Fig. 6.—Carcinoma of the upper central part of the breast with pronounced retraction signs. Note the deep dimple over the carcinoma, the contraction of the areola and the pulling up of the nipple toward the lesion.

following it from the anterior axillary fold to the midline on each side. An indentation or a bulge in this contour often betrays the site of a lesion. He compares the height of each breast on the chest wall and their relative size.

The shrunken breast of advanced slowly growing carcinoma, or the generally enlarged edematous breast of acute carcinoma are at once obvious, but the subtle changes due to earlier lesions are not so evident.

It will sometimes be noted that one breast is slightly larger than the other, yet perfectly symmetric with its mate. This mere disparity in size is often only a developmental defect, and if not accompanied by other signs is no cause for alarm.

The shape and size of the areolas and their comparative level are next studied. The shape of the nipples and the axes in which they point are compared. The surface of the nipples is carefully inspected in a search for crusting or erosion.

Inspection completed, the examiner is ready for palpation of the breasts. This is best performed with the patient lying down (fig. 5). For adequate palpation the breast should be balanced on the chest wall, forming an even layer spread out over the thoracic cage. To achieve this we elevate the chest on the side of the breast being examined by placing a small pillow under

the shoulder. If the breast is allowed to fall to the patient's side, folding on itself, the examiner may mistake its folds for abnormalities.

The whole extent of the breast is now gone over with the tips of the fingers. It should be kept in mind that the breast tissue often extends over a wide area. A thin layer of it may reach the midline of the sternum medially, the lower edge of the clavicle above and the edge of the latissimus dorsi muscle laterally. Small subcutaneous tumors near these outer limits of the breast may be mistaken for benign subcutaneous lesions not associated with the breast when in fact they are carcinomas of the breast. The axillary prolongation of the breast extends high into the axilla in some subjects, and carcinoma arising in it is commonly mistaken for lymphosarcoma or adenitis of the axillary lymph nodes.

In palpating the breast a little talcum powder on the skin diminishes friction and may add to the accuracy

Fig. 7.—Carcinoma of the upper outer sector of the breast. Note the broad dimple over the carcinoma and the pulling up of the nipple toward it.

of tactile perception of the consistence of breast tissue. Gentle palpation is not only more informative than rough examination; it is a necessary precaution against the hazard of causing metastasis. We try to emphasize this danger by sharply limiting the examination of women with carcinoma of the breast by students on our wards.

Although palpation in the supine position is certainly the best method of detecting abnormalities in most parts of the breast, there is one area which it is wise also to palpate between the fingers of both hands with the patient sitting up. This is the subareolar and nipple region. In this central area where the ducts converge to enter the base of the nipple the breast structure is looser and less dense. In breasts which are thick and relatively firm in texture, the comparatively dense breast tissue forms a sort of ledge around the softer subareolar region. The cephalad portion of this ledge is not infrequently mistaken for a tumor. On the other hand, a real tumor of small size situated in the softer subareolar area may be almost impalpable in the supine position, although when examined between the fingers with the breast dependent the tumor is readily felt.

It has been our experience that careful palpation of the breast, carried out according to this plan, will reveal a carcinoma of the breast even when it measures only 4 or 5 mm. in diameter. The hardness of the tumor and its relative fixation in the area of breast tissue in

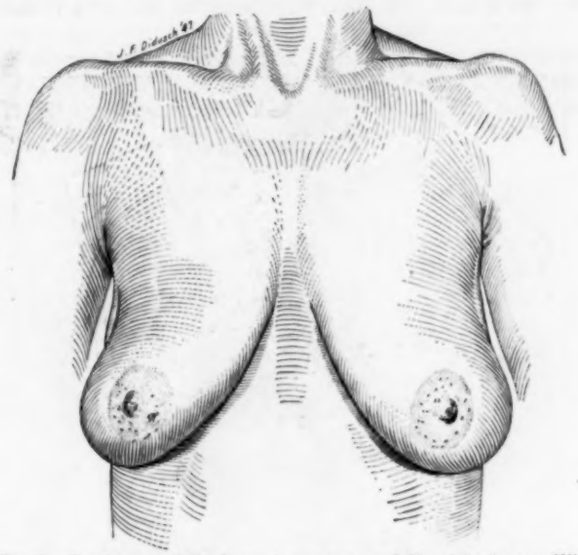

Fig. 8.—Carcinoma of the lower inner sector of the right breast. With arms at the sides no asymmetry is seen.

which it lies, making it impossible to move it without carrying along the surrounding breast tissue, are the features which most often suggest that it is a carcinoma. Most carcinomas are not sharply circumscribed; the edge of the lesion merges with the surrounding breast tissue which it infiltrates. This makes a carcinoma difficult to measure precisely.

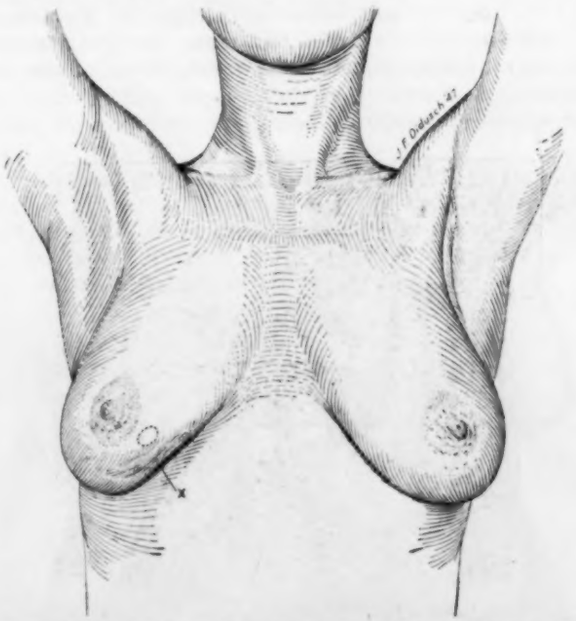

Fig. 9.—Carcinoma of the lower inner sector of the right breast. With arms raised an indentation is seen at X.

But consistence and mobility and circumscription are by no means reliable indications of the nature of a tumor of the breast. Papillary carcinomas and colloid carcinomas may be soft, while a calcified fibroadenoma may be as hard as stone. There is a type of strikingly well circumscribed carcinoma which we call in our laboratory the *solid circumscribed type*, which may strongly suggest a cyst or a fibroadenoma. On the other

hand, cysts which have ruptured and have set up an inflammatory reaction in the surrounding breast tissue may be as much fixed in the breast as a carcinoma. There are many other exceptions to these rules.

Fig. 10.—Lifting up the breast to demonstrate a dimple at X over a carcinoma in the upper central part of the breast.

Retraction Phenomena.—A greater reliance in diagnosis can be placed on the retraction phenomena which carcinoma almost always produces in the breast. When the examiner has completed his palpation of the breast he should turn his attention to a search for these retraction signs. They constitute a whole series of clinical

Fig. 11.—Gentle compression of the breast to demonstrate a dimple over a carcinoma in the upper sector of the breast.

signs ranging from the simple dimple in the skin over the tumor to shrinkage of the entire breast. They are due to the fact that as carcinoma grows it causes proliferation of fibroblasts not only within its own structure but in the surrounding breast tissue. This scar tissue, so to speak, contracts as it grows older, and since the breast is normally loose and fatty in structure, any or all of the tissues surrounding the carcinoma may be pulled in toward it by the shortening strands of fibroblasts. This phenomenon is of fundamental importance in the interpretation of the clinical signs that the disease produces.

A good example of pronounced retraction is illustrated in figure 6.[2] Here the carcinoma is situated in the upper central portion of the breast just above the areola. The skin over it has been drawn inward,

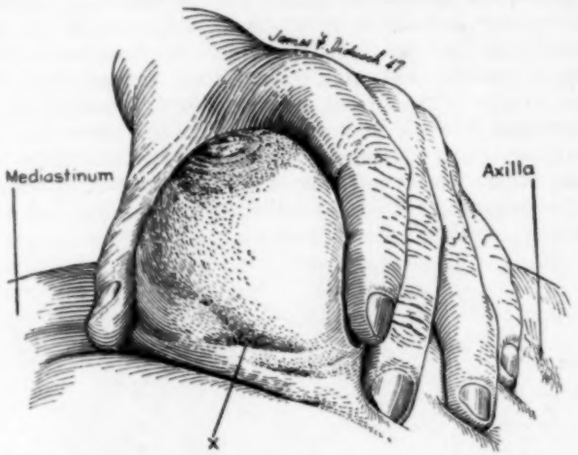

Fig. 12.—Gentle compression of the breast to demonstrate a dimple over a carcinoma in the lower part of the breast near the inframammary fold.

forming a deep dimple. The areola has been pulled upward toward the carcinoma, and in its upper part it is so narrowed that it is hardly discernible. The nipple is flattened and is also pulled upward toward the carcinoma. The nipple and areola may be said to point toward the carcinoma.

Fig. 13.—Carcinoma of the upper outer sector of the left breast. The arms rest relaxed on the patient's hip and no retraction signs are seen over the lesion.

Another example of a dimple in the skin over a carcinoma of the breast is shown in figure 7. Here the dimple is a broad, shallow one. Again the areola and the nipple are pulled upward toward the carcinoma.

2. All of the drawings used to illustrate this article have been drawn by Mr. James F. Didusch from actual photographs.

Usually these retraction signs are less well developed. In small early carcinomas they are often, indeed, so subtle that they can only be demonstrated by certain maneuvers.

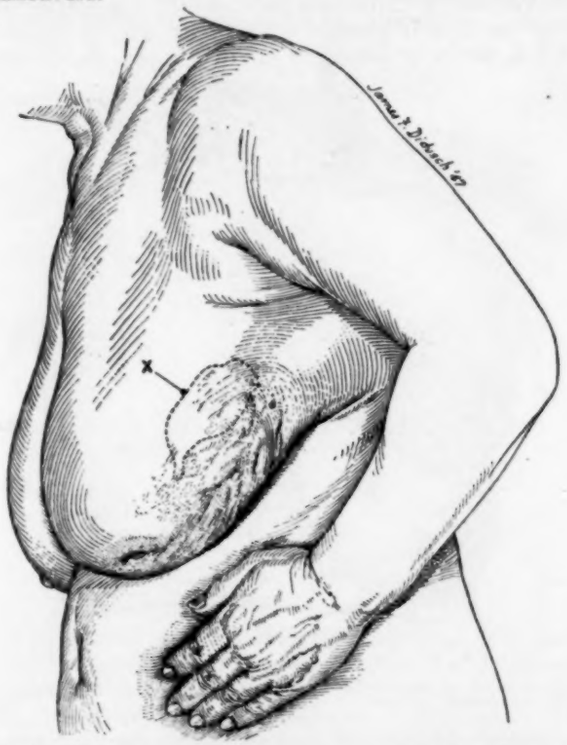

Fig. 14.—Carcinoma of the upper outer sector of the left breast. The arm is pressed against the side contracting the pectoral muscles and bringing out pronounced skin retraction.

The simple act of raising the arms high above the head will sometimes reveal asymmetry of the breasts, or retraction of the skin, which is of decisive diagnostic significance. Figure 8 shows a 30 year old patient in whom no asymmetry of the breasts is evident as she sits with her arms at her sides. In figure 9, which shows

Fig. 15.—Testing the lateral movability of the breast.

her with her arms raised, a well defined indentation is seen in the inner lower sector of the right breast at the region marked X, adjacent to the small tumor indicated by the circle. As this evidence suggests, the tumor proved to be a carcinoma. The fibrosis around the carcinoma has attached it abnormally closely to the underlying pectoral fascia and to the overlying skin. When the arms are raised, elevating the pectoral fascia, the carcinoma and the overlying skin are pulled upward and inward to a greater degree than the surrounding normal breast, producing the telltale asymmetry.

Another maneuver that is useful in revealing retraction of the skin is for the examiner to lift the breast upward with his hand, as in figure 10. When the carcinoma is in the upper half of the breast this maneuver will often bring out a dimple in the skin over it, as at the point marked X in the figure. The mechanism of this phenomenon is a simple one. The skin over

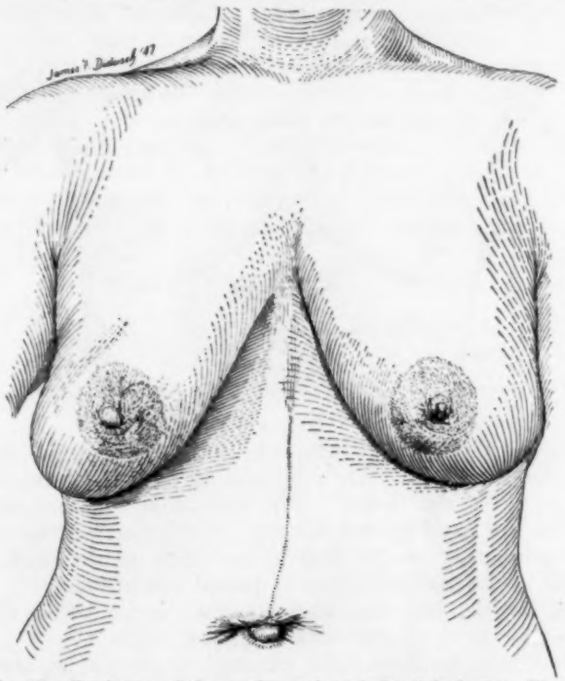

Fig. 16.—Carcinoma of the areolar region of the right breast. Breasts symmetrical in erect position.

the carcinoma is held down by the abnormally shortened connective tissue strands between it and the carcinoma, while the skin over the normal surrounding breast lifts freely.

A variant of this lifting maneuver is gentle compression of the breast on both sides of the carcinoma as in figure 11. Here again a dimple develops at X over the lesion in the upper outer sector of the breast, while the surrounding skin bulges normally.

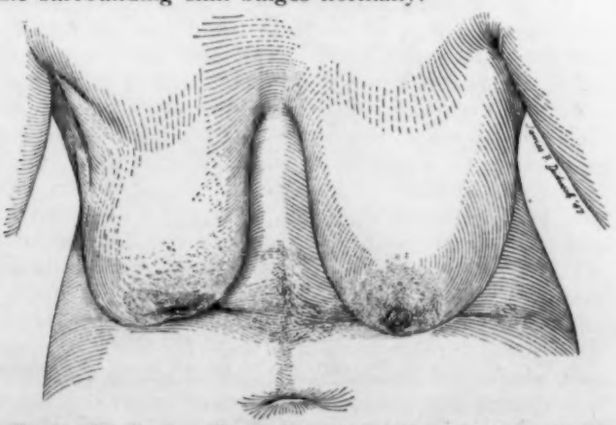

Fig. 17.—Carcinoma of the areolar region of the right breast. In forward bending position the areolar region is deeply retracted.

When the carcinoma is in the lower half of the breast this same maneuver, carried out with the patient lying down, will often bring out a dimple over the lesion, as shown at X in figure 12.

A maneuver which is often helpful in demonstrating retraction signs in a carcinomatous breast is that of pectoral contraction. While in the sitting position the patient relaxes and rests her hands on her hips, giving the examiner an opportunity to compare the relative

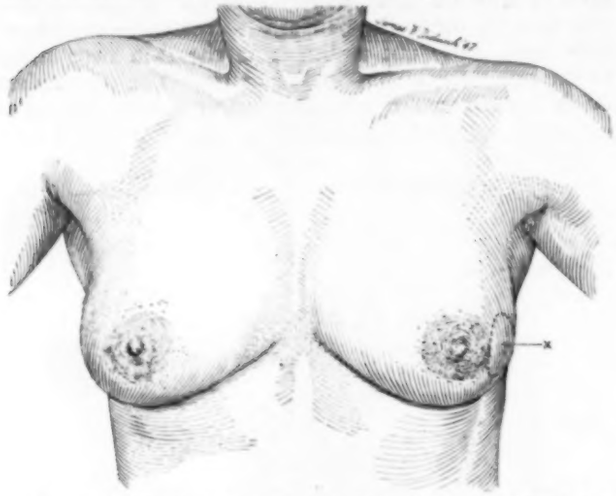

Fig. 18.—Carcinoma of the outer part of the left breast. Breasts symmetrical in erect position.

heights of the lower edge of the breast and the level of the areola on each side, and to look for retraction signs over the tumor. The patient is then asked to press her hand against her hip, contracting her pectoral muscles, first on the normal and then on the diseased side. The normal breast is pulled upward slightly by this action, but the carcinomatous breast often rises sharply as compared with its mate. The breast as a whole may be abnormally elevated, or merely the sector of the breast in which the carcinoma is situated. This abnormal elevation occurs, of course, because the fibrosis in the carcinomatous area ties it down to the underlying pectoral fascia. When contraction of the pectoralis major elevates the pectoral fascia the carcinomatous area in the breast is pulled up with it. This is a *relative*, not a *solid*, fixation, as when carcinoma in a more advanced stage becomes immobile on the chest wall.

Fig. 19.—Carcinoma of the outer part of the left breast. In forward bending position there is flattening of the lateral contour of the breast at X.

When the carcinoma is solidly fixed, pressing the hand against the hip of course produces no elevation of the breast at all.

Pectoral contraction also brings out other retraction signs—deviation of the nipple toward the carcinoma, and lines and dimples in the skin over it. Figures 13 and 14 demonstrate this pectoral contraction maneuver in a patient with carcinoma in the outer upper part of the breast. Figure 13 shows the patient with her arm relaxed: no definite dimpling is seen in the skin adjacent to the carcinoma indicated by the circle. But when her arm is pressed against her side in figure 14 a whole series of lines and furrows appear in the skin.

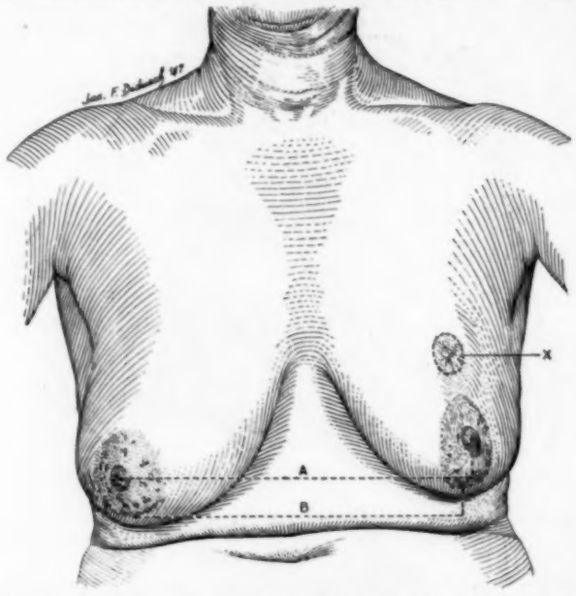

Fig. 20.—Carcinoma of the upper central part of the left breast. Left areola and nipple elevated.

Another method of demonstrating the presence of a relative degree of fixation of the carcinomatous area in the breast to the pectoral fascia is to test the lateral

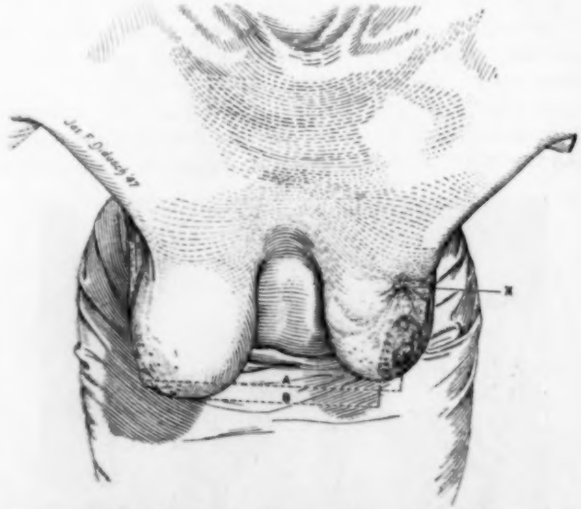

Fig. 21.—Carcinoma of the upper central part of the left breast. The elevation of the areola and the nipple, and the breast as a whole, are accentuated by forward bending.

mobility of the breast while the patient lies supine, as shown in figure 15. In the gentlest possible manner the sector of the breast containing the tumor is moved transversely across the chest wall between the fingers of the examiner's two hands, first with the arm relaxed, and then with the arm pressed against the hip to contract the pectoral muscles. In patients in whom the diseased area is relatively fixed by fibrosis to the underlying pectoral fascia the breast can be moved freely while the arm is relaxed, but motion is sharply checked when the pectoral muscles are contracted.

Another procedure of great value in demonstrating retraction signs in the breast is the forward bending

maneuver. I learned of it from the late Hugh Auchincloss, who used it with striking effect. The patient is asked to bend far forward from the hips, keeping her chin up and extending her hands forward to the examiner who supports them as he sits before her. In this

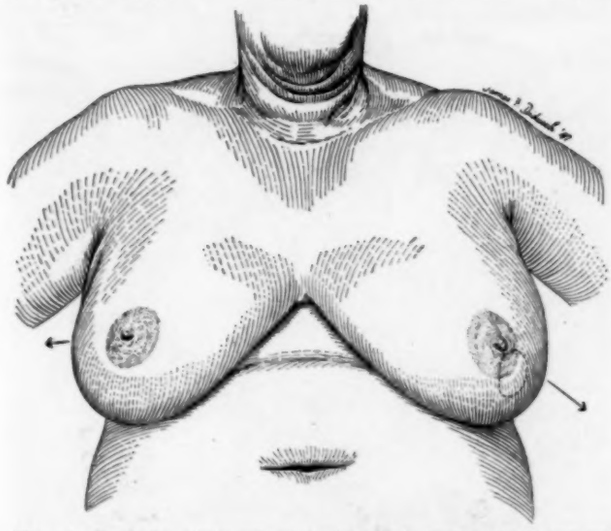

Fig. 22.—Deviation of the axis of the left nipple downward and outward toward a carcinoma in the lower outer sector of the breast.

position normal breasts fall freely away from the chest wall and are perfectly symmetrical. But if a carcinoma is present in one of them, even though the growth be small, the fibrosis which accompanies it will usually fix in some degree the diseased breast to the chest wall and produce an asymmetry which careful inspection from the side or from the front will detect. Over and over again we have seen carcinoma in the breast betrayed by asymmetry demonstrated by this maneuver, although there were no other retraction signs. Figures 16 and 17 show a good example of the value of forward bending. There was a small firm carcinoma beneath the areola as indicated by the circle, but no asymmetry was evident as the patient sat with her arms at her sides.

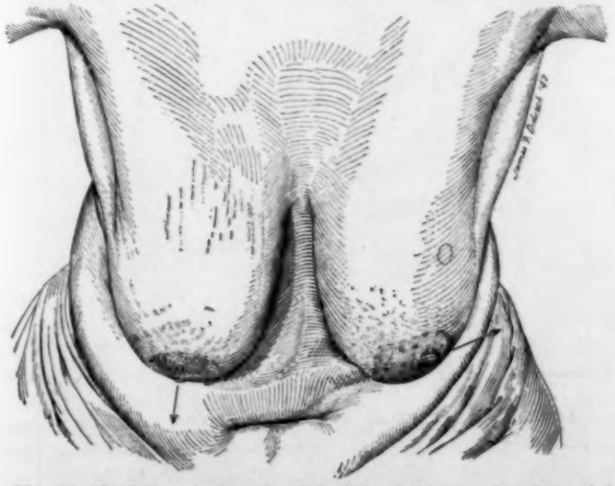

Fig. 23.—Deviation of the axis of the left nipple upward and outward toward a carcinoma in the upper outer sector of the breast, accentuated by forward bending.

When she bent forward, however, the nipple and medial part of the areola were pulled deeply up into the breast. No observer would miss this distortion.

The change in the contour of the breast which carcinoma produces is much less apparent in some cases. The patient shown in figures 18 and 19 illustrates this fact. Here forward bending revealed only a slight flattening of the lateral contour of the left breast in the area marked X adjacent to the carcinoma indicated by the circle. There was no dimple in the skin over this lesion.

In his search for retraction signs the examiner should pay special attention to changes in the areola and nipple. The horizontal level of the areola and nipple is often elevated by a carcinoma in the upper half of the breast. The areola may be narrowed and distorted so that it points toward the carcinoma All these changes are illustrated in figure 20. They were accentuated when the patient bent forward as shown in figure 21.

Deviation of the axis in which the nipple points is a subtle variety of retraction sign. The fibrosis in and about the carcinoma pulls on the duct system and tilts the nipple so that it points toward the carcinoma. Figure 22 shows deviation of the axis of the left nipple downward toward the carcinoma indicated by the circle in the lower breast. Figure 23 shows upward deviation

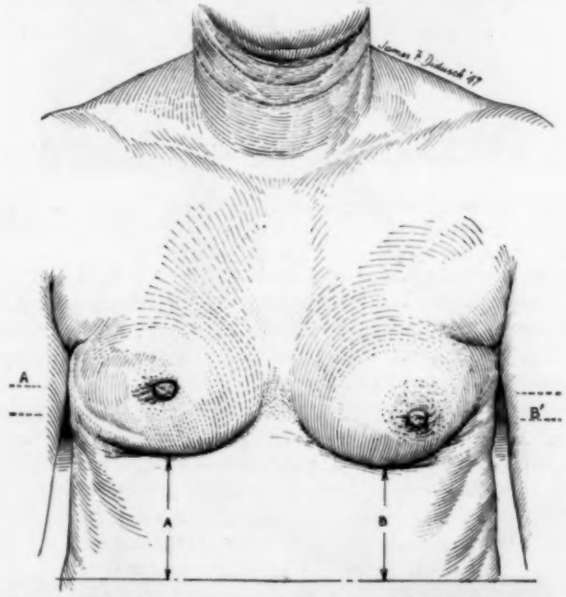

Fig. 24.—Flattening and broadening of the right nipple due to a carcinoma in the central part of the breast.

of the left nipple toward a carcinoma indicated by a circle in the upper part of the breast. In this figure the deviation is accentuated by forward bending.

When the carcinoma involves the area more or less directly beneath the nipple the fibrosis shortens the whole duct system and pulls the nipple inward. This process may show itself merely as flattening and broadening of the nipple (fig. 24) on the carcinomatous side as compared with its mate. The nipple loses its elasticity and cannot be pulled out like the uninvolved one. As the fibrosis progresses the nipple becomes flatter and broader until, in some instances, it finally retracts beneath the surface of the surrounding areola (fig. 25).

Flattening or retraction of the nipple due to carcinoma should not be confused with mere inversion of the nipple, a condition seen in a good many women with no disease of the breast. Inversion of the nipple may be bilateral or unilateral. The patient will usually say that the inversion has been present for many years and that it interfered with nursing. Instead of protruding in the normal way the inverted nipple has the appearance of a sulcus, into the bottom of which the ducts open. Inverted nipples can often be pulled out. They are not broadened and thickened and fixed, like the retracted nipple of carcinoma.

The fibrosis following an abscess sometimes distorts the nipple, changing its axis or inverting it. The history and the presence of a scar should enable the examiner to interpret such changes correctly.

The carcinomas of the breast in which a careful examination fails to reveal any of the retraction signs described are few indeed. In my experience these few have been either the solid circumscribed type or well differentiated types. Both of these varieties seem on occasion to produce less fibrosis in the surrounding breast than most carcinomas, and therefore less retraction.

Erosion.—Erosion of the surface of the nipple is an important sign of carcinoma. Even when it is only 2 or 3 mm. in diameter it warrants a presumptive diagnosis of the Paget type of carcinoma. Modern histologic studies have shown that what Sir James Paget thought was a "disease of the mammary areola preceding cancer of the mammary gland" is in fact actual involvement of the nipple epidermis by carcinoma cells. In Paget's erosion of the nipple meticulous microscopic search of the breast will always reveal somewhere in it a primary carcinoma whose cells have grown along the ducts to reach the surface of the nipple. These so-called Paget cells have a peculiar predisposition to grow only within the epidermis (fig. 26). Not all erosions of the nipple, of course, are carcinomatous, for inflammatory and trophic eczema-like lesions do occasionally develop in the nipple and areola. But the percentage of nipple erosions that are carcinomatous is so high that biopsy of the lesion and microscopic proof of its nature are always necessary. The typical Paget erosion is a crusted or moist and granular area on the surface of the nipple (fig. 27). It dries up and seems to heal over from time to time but soon breaks open again, enlarging slowly but steadily. The nipple is flattened and finally destroyed by the process, which extends onto the areola and then over the skin of the breast. This type of carcinoma is relatively somewhat less malignant than other forms of carcinoma of the breast, and cure may be achieved even when the erosion has been present for years and has involved a large area of the skin over the breast, as in the patient shown in figure 28.

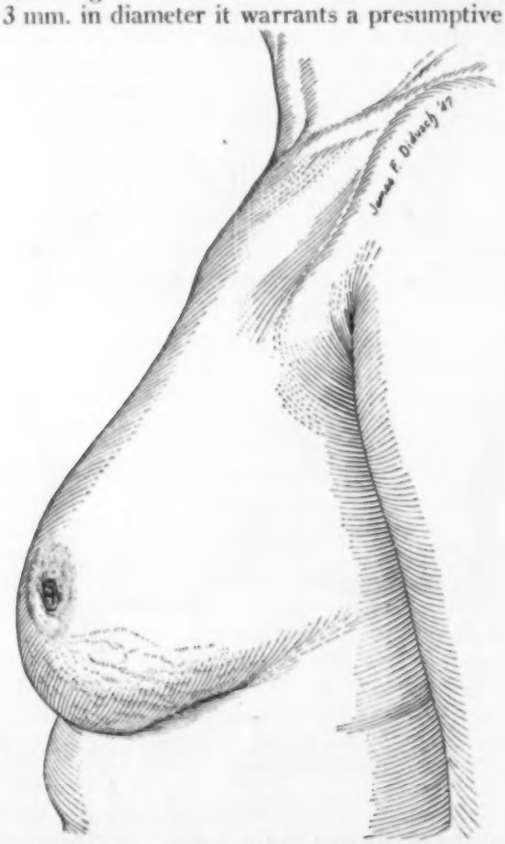

Fig. 25.—Side view of the left nipple showing it retracted below the level of the areola due to a central carcinoma of the breast.

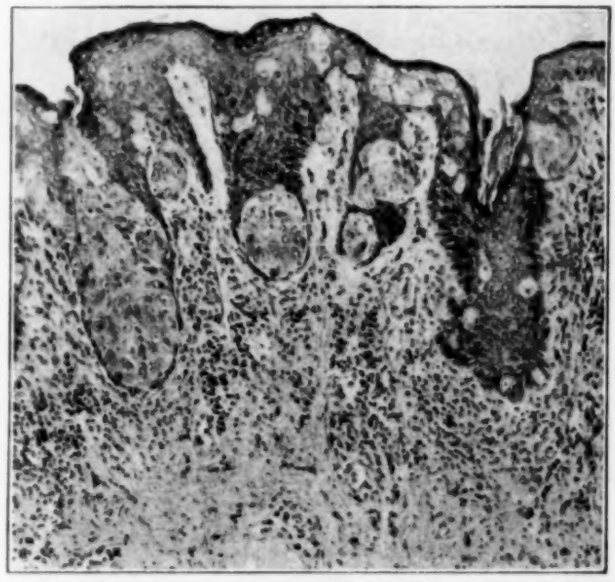

Fig. 26.—Paget carcinoma cells in the epidermis of the nipple.

Discharge.—A discharge from the nipple is, of course, a sign of abnormality in the breast. This may be physiologic and harmless, or pathologic and an indication of inflammation or of epithelial proliferation. The character of the discharge is an important distinguishing feature.

Fig. 27.—Paget's erosion of the nipple—an early lesion.

A discharge which has the consistency and color of milk is usually just that. Occasional women continue to secrete a small amount of milk for months, and in rare cases for years, after lactation would normally have ceased. We do not yet have enough understanding

of the hormonal control of lactation to know the physiologic mechanism in these cases. This kind of nipple secretion is usually bilateral. The few drops of milk that accumulate in the duct system of such a breast do not usually escape spontaneously but appear only when the breast is squeezed or the nipple is stimulated. Such a discharge from the nipple is harmless.

Low grade inflammatory processes, developing in the subareolar portion of the breast close to the larger ducts, sometimes break into a duct which provides a channel for the escape of secretion. This type of inflammatory discharge has the gross character of pus, and its nature can be confirmed by making a smear of it and examining it microscopically. Although recurring or persisting infection in the breast is notoriously difficult to eradicate, perhaps because of the poor blood supply and fatty character of the breast tissue, attempts to provide adequate surgical drainage should be made in these cases. When the abscess cavity is opened it is wise to excise a small piece of tissue for microscopic examination, to rule out the possibility of unsuspected carcinoma.

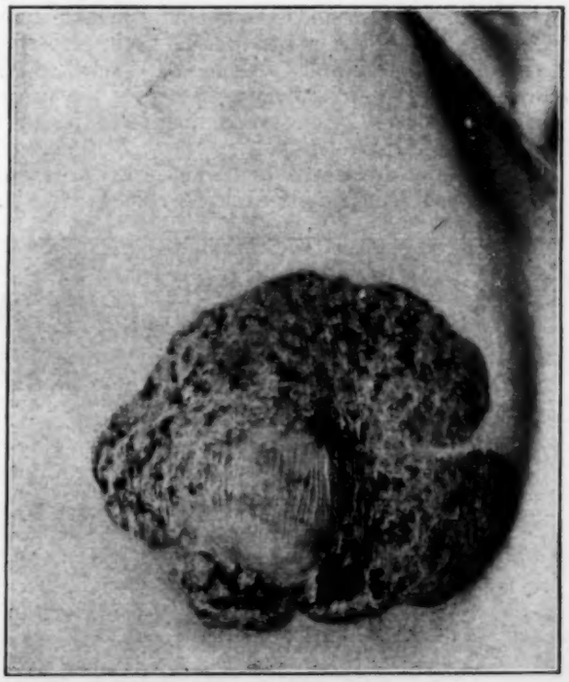

Fig. 28.—Extensive Paget's disease with destruction of the nipple.

A thin, yellowish, brownish, reddish or frankly bloody discharge from the nipple is almost always a sign of epithelial proliferation. This kind of discharge usually escapes spontaneously and stains the patient's brassière. In the great majority of cases it is due to an intraductal papilloma growing in one of the larger ducts in the subareolar region, and not to carcinoma. The dilated duct containing the papilloma can usually be detected by careful palpation as a small cordlike or rounded tumor beneath or close to the areola. Pressure on it produces a drop or two of secretion from the opening of the involved duct on the surface of the nipple. Such a lesion should always be explored surgically, and the diseased duct or ducts excised. Microscopic examination will confirm the benign nature of the papilloma and rule out carcinoma.

If the papillary process is situated some distance out in the breast tissue away from the subareolar region, or if it has grown to form a tumor of considerable size, it is wise to make a biopsy of the lesion before attempting to remove it, because such growths are often papillary carcinomas.

If, in a patient with a history of a yellowish, brownish or bloody discharge from the nipple, careful palpation

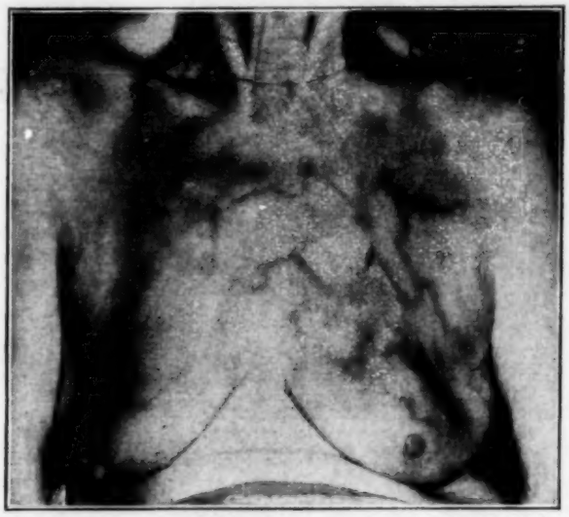

Fig. 29.—Infra-red photograph to show dilated subcutaneous veins in carcinoma of the left breast.

does not reveal any tumor or any point where pressure elicits the discharge, the surgeon should reexamine the breast after a few days, cautioning the patient against squeezing the breast in the meantime. During this interval the secretion will have an opportunity to accumulate in the diseased duct, and reexamination may localize it.

When examination still fails to reveal the source of the discharge the subareolar and central area of the breast should be explored surgically. Although difficult for the surgeon, such an exploration is justified

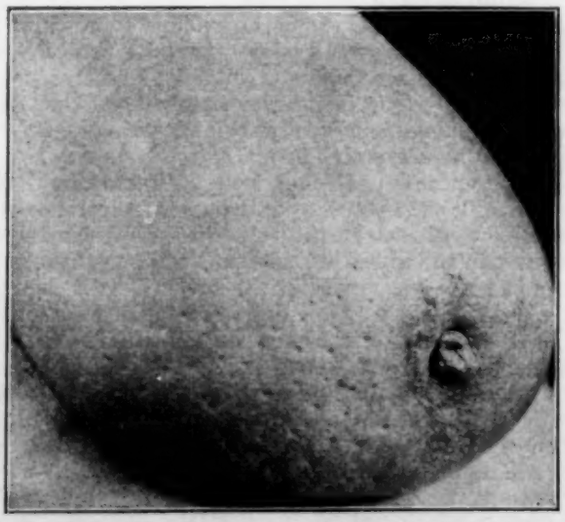

Fig. 30.—Extensive edema of the skin in carcinoma of the breast.

because this type of discharge from the nipple is in a small percentage of cases a sign of carcinoma.

Only about 5 per cent of carcinomas of the breast are, in fact, accompanied by a discharge from the nipple. In most of these patients there is also a palpable tumor which has the clinical characteristics of a carcinoma.

The discharge is more often frankly bloody than yellowish or brownish. Even though it is infrequently the only sign of carcinoma, such a discharge from the nipple should never be dismissed lightly. Its cause must be searched for and its nature proved.

Abnormal Circulatory Relationships. — Retraction signs are not, of course, the only clinical signs produced by carcinomas of the breast. There is a group of

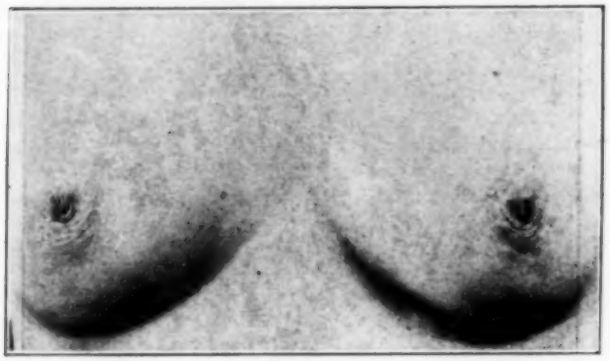

Fig. 31.—Edema limited to the skin of the areolar region in carcinoma of the right breast.

clinical signs produced by abnormal circulatory relationships in the breast. Carcinoma growing in the breast causes an increase in the blood supply to the part. This not infrequently produces hyperemia of the skin, which is abnormally warm and sometimes reddened. The subcutaneous veins over the upper part of the breast may be visibly dilated. Infra-red photographs bring out this dilatation in a striking manner (fig. 29). At operation the internal mammary vessels (the chief blood supply to the breast) at the intercostal level corresponding to the carcinoma will often be seen to be abnormally large. It may be argued that prominence of subcutaneous and intercostal veins might be due to venous obstruction, but we have repeatedly seen it in cases in which there was no evidence at all of obstruction of the axillary vein.

Edema of the skin of the breast due to blocking of the subdermal lymphatics is an important sign of carcinoma in an advanced stage. Lymph accumulates within the skin until it is several times its normal thickness, and causes abnormal separation and deepening of the orifices of the cutaneous glands (fig. 30).

When the area of edema is small, as in the case shown in figure 31, it easily escapes detection unless carefully looked for. It usually begins as in this patient, in the skin within the areola, or just caudad to it; that is, in the most dependent part of the breast. This is regularly the site where edema appears when the carcinoma is situated deep in the center of the breast, but it may also be the earliest location of edema when the carcinoma is situated in the periphery of the breast. We have seen edema appear just below and medial to the nipple when the carcinoma was a small one located in the extreme upper outer part of the breast.

This tendency of edema to develop in the areolar region is probably due to the fact that carcinoma of the breast tends to spread, in its late stages, in a retrograde fashion along the main lymphatic pathways. These radiate from the areolar region.

There are, of course, other cases in which the edema first appears in the skin immediately over a carcinoma situated more peripherally in the breast. In such cases the skin is usually somewhat adherent to the underlying tumor, and it seems probable that the lymphatics of the skin are obstructed by direct retrograde invasion from the surface of the growth outward.

We have been much interested in the mechanism by which edema of the skin is produced, and we have made a special effort over a period of years to study the skin histologically in these cases. In interpreting the findings the first requisite, of course, is an appreciation of the normal arrangement of the lymphatics in the skin. There are no lymphatics in the epidermis itself. In the corium, however, there are two networks of them, a narrow-meshed superficial subdermal one which sends branches up around the papillae, and a wide-meshed deeper one made up of broader channels equipped with valves which communicate by means of vertical branches with the subdermal lymphatics. Our histologic studies of edematous skin have led us to the conclusion that the process begins with the appearance of embolic masses of carcinoma cells in the deep network of lymphatics in the corium. We believe that the mechanism by which extension takes place is at first embolic, rather than one of continuous permeation, because we have often seen the picture illustrated in figures 32 and 33. Here, in edematous skin, the deeper lymphatics are dilated and contain unmistakable tumor emboli. As the edema progresses both the superficial and deep lymphatic vessels become solidly choked with tumor cells, and at this advanced stage of the process permeation is probably the predominant mechanism by which the disease extends.

These signs of disturbed circulation in the breast are, of course, also seen in infections in the breast, both

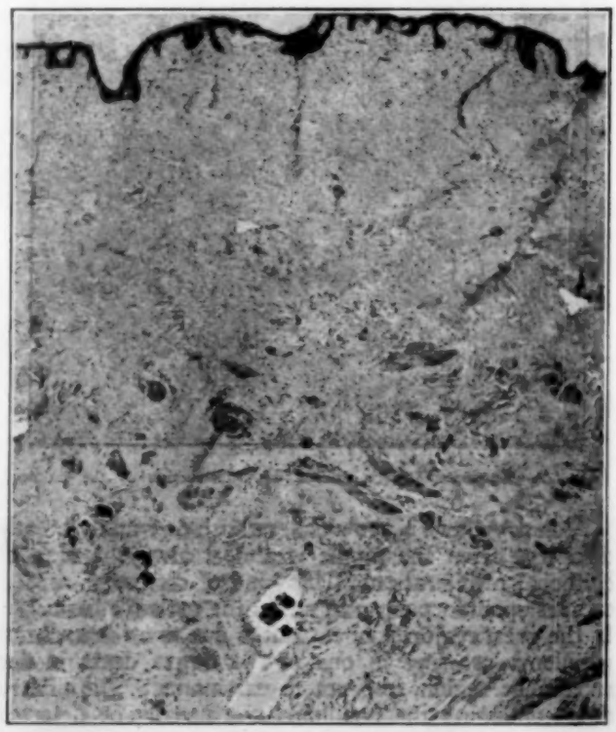

Fig. 32.—Photomicrograph of edematous skin in carcinoma of the breast, showing carcinoma emboli in dilated subdermal lymphatics.

in acute abscesses and in low grade chronic infections. They are not as distinctive of carcinoma as the retraction signs. Both classes of signs, moreover, may be produced by entirely benign lesions.

Transillumination.—Transillumination of the breast has been emphasized by some clinicians, but we have found it to be of such limited usefulness that we do

not employ it routinely. A papillary cystadenoma containing bloody fluid, situated in the subareolar area of a dependent breast, will show up well in transillumination as a sharply circumscribed entirely opaque shadow. But even when it gives this picture transillumination does not rule out carcinoma and further diagnostic steps are necessary.

Roentgen Examination.—Examination of the breast by roentgen rays to show changes in soft tissue density is not, in our opinion, of any definite value, and we do not employ it. The injection of the ducts of the breasts with an opaque medium for roentgen study seems to us a dangerous procedure. The ducts may contain carcinoma, and injection may distend and rupture them and force carcinoma cells into veins and lymphatics.

All of the refinements of clinical diagnosis which I have described may, of course, be said to be of academic importance, because one cannot lay down absolute rules regarding the diagnostic significance of even the most

Fig. 33.—Higher power view of dilated subdermal lymphatic vessel containing carcinoma emboli.

reliable clinical signs. The surgeon who performs a radical mastectomy must be absolutely certain of his diagnosis, and clinical signs give such security only when they are well developed and when they are interpreted with an extensive background of experience. In most cases the surgeon will wish to rely on the microscopic proof of the presence of carcinoma, for he knows that there are a whole series of benign lesions of the breast which simulate carcinoma more or less closely. A low grade abscess, traumatic fat necrosis, a cyst whose contents have in part escaped into the surrounding breast tissue and set up an inflammatory reaction, adenosis, myoblastoma—any of these may form a hard tumor in the breast with dimpling of the overlying skin. The surgeon's dilemma is a difficult one. He must have proof of the nature of the lesion with which he is dealing, for his whole plan of treatment hinges on this one fact. The benign lesions require only simple local excision, while carcinoma demands a formidable and mutilating operation which must never be done needlessly.

(To be continued)

Clinical Notes, Suggestions and New Instruments

HAZARDS OF CURARE

Presentation of a Case

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and
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With the increase in the various "shock therapies," both in institutions and in the private offices of the nation's psychiatrists, there is bound to be an increase in the absolute number of fractures, pulmonary abscesses and deaths, as well as other complications. The literature is replete with case studies of patients with varied diagnoses who have shown adequate and early response to shock therapy. With the improvement of technic and the institution of electroconvulsive treatments have come refinements in procedure which, on the whole, have tended to ameliorate the complications and to increase the number of patients who are being treated. Electroconvulsive therapy has almost completely supplanted the use of "metrazol" N. N. R. (pentamethylenetetrazol) and is tending more and more to supplant insulin therapy. Patients with the depressions and other affective disorders who respond to "metrazol" therapy respond more quickly and with greater ease to the electrical form of convulsive stimulation. More patients can be treated at the same time, and the safety factor is much greater. No longer does one see the severe fractures previously noted with "metrazol" therapy, nor is it as difficult to gage the amount of electrical potential necessary as it was to gage the amount of chemical to be injected. Few therapists are willing to expose their patients to the greater dangers and the lesser certainty of "metrazol" therapy, when they have at hand the simple, less costly and safer procedure which is possible with the electroshock machine. Although the delusional patient does not respond too well to electroconvulsive therapy, his response seems to be equal to the response to insulin therapy, so that again electroconvulsive therapy is the method of choice.

Fractures still form the basis for the greatest fear in the mind of the therapist, and in order to obviate these he has resorted to manual, instead of mechanical, restraint and hyperextension of the dorsolumbar aspect of the spine. These improvements are still too inadequate to prevent fractures completely in certain patients, e.g., muscular men. In addition, there are those patients whose mental condition is sufficiently severe to warrant convulsive therapy but who have bony changes which increase the chances for fracture. Many attempts have been made to lessen the severity of the convulsion among these persons. They have been sedated or have been completely narcotized with preliminary barbiturate medication by either the oral or intravenous route. Various other anticonvulsants have been utilized, none of which proved adequately effective except curare.

With the introduction of treatment with curare, many patients, who otherwise could not be treated because of fear in the mind of the therapist that fractures might ensue, have been accepted for convulsive therapy, with results which justify the use of this added hazard. Some patients have had treatment continued despite vertebral fractures if the psychiatric prognosis justified continued treatment. The usual procedure is to fix the area involved in a cast and to give an injection with curare prior to the advent of further convulsions. Here, too, the results have been favorable and have justified this comparatively radical procedure. The patients, on improvement or recovery from their mental illness, have usually been asymptomatic regarding the injury to the spine.

Read at the Down-State Psychiatric Meeting of the New York State Department of Mental Hygiene, New York State Psychiatric Institute, April 21, 1948.

REPORT OF A CASE

The following report is of a 25 year old white woman with a diagnosis of dementia praecox, catatonic type, who, because of a right femoral hernia which increased in size with each convulsion, was given curare medication. Although she had been mentally sick for a year and a half prior to treatment, the results of three electrically induced grand mal seizures were sufficiently promising to warrant continued treatment despite the additional hazard occasioned by curare medication. Unfortunately, the patient's reaction to curare was poor, and it was felt that her death, following the ninth treatment, was precipitated by treatment with this drug. The preparation used was a product of E. R. Squibb & Sons, "intocostrin"—curare in aqueous diluent—with a standard concentration.

S. A., the daughter of a shy withdrawn father and an aggressive domineering mother, whose family history revealed no evidence of nervous or mental disease, was admitted to the Rockland State Hospital on Feb. 14, 1946, because she would sit motionless, staring fixedly. She paid no attention to questions asked, but at times would giggle inappropriately. She was subject to delusions and hallucinations and showed apparent defects of insight and judgment. She had recently been discharged from another psychiatric hospital, where she had remained for ten months and had received some electroconvulsive therapy and some insulin therapy, with improvement, which was, however, not maintained. She was discharged from this previous institution in December 1945, with her condition noted as "unimproved." For a period of three months she was kept at home, but, because of the difficulty of caring for her, she was admitted to Rockland State Hospital.

The patient was a wanted child, born by normal spontaneous delivery, after an uneventful pregnancy, on Feb. 25, 1921. Early development was described as having been uneventful until the age of 5. At this time the patient refused to leave her mother long enough to attend kindergarten. She retired more and more from external contacts, daydreamed a great deal and preferred reading to mingling with other children. Despite her propensity for reading, she did poorly in school and lost one or two grades. At the age of 16 she left high school to attend business school. She learned to type and at 18 years took her first job as a typist. She worked intermittently, never holding any job more than several weeks. She continued in this fashion until the onset of her present illness.

Her medical history was uneventful. Menarche appeared at 14 years, without untoward distress. She was somewhat disturbed when her breasts failed to develop and wore brassieres stuffed with cotton to hide this development defect. She never showed interest in boys or approved of cosmetics or bad language. She neither smoked cigarets nor drank alcoholic beverages. During the night of Feb. 2, 1945, the patient awoke weeping uncontrollably. She protested that nothing was wrong and that her behavior was caused by a "bad dream." Thereafter she began to sit around, staring into space, and was apparently depressed. She persistently denied that anything was wrong, but had frequent spells of uncontrollable weeping. On February 15 she was admitted to the New York Psychiatric Institute and Hospital. Physical examination here revealed an asthenic, young adult, white woman with subnormal breast development and a large right femoral hernia in her groin, with a swelling the size of a hen's egg. There was a harsh systolic murmur at the cardiac apex, but the electrocardiogram was normal. All other physical observations were normal, and results of laboratory procedures were negative. Mentally she was listless, showed decreased motor activity and decidedly constricted mental activity. Her emotional reaction suggested tension and depression. She manifested ideas of reference with many persecutory trends—people were watching her and talking about her and accused her of having a love affair and of being a "bad" girl. She blocked in answering questions referring to sexual matters. The sensorium was intact, but mental grasp and capacity were below normal. The Kent EGY test score was 14 and her intelligence quotient 67. Judgment and insight were very poor.

During her stay at the Psychiatric Institute and Hospital she received ambulatory insulin therapy combined with electroconvulsive therapy, resulting in some well defined improvement. She seemed to be in better contact, was less suspicious and joined with other patients in ward activities. The bizarre hallucinations and delusions which were previously apparent tended to disappear. Unfortunately, she regressed and again became rather seclusive, negativistic and demanding. She showed utter lack of judgment and again manifested auditory hallucinations and delusions. She laughed and wept alternately in response to her hallucinations. Therefore, insulin coma therapy was instituted which was terminated on November 10, at which time the patient had received thirty-three treatments, resulting in twenty-nine comas. She showed no improvement in her mental attitude and was discharged on December 12 as "unimproved."

A few months later this girl was admitted to the Rockland State Hospital. She was given a course of electroconvulsive therapy immediately on admission and received a total of twenty applications, resulting in twenty grand mal seizures, but with no noticeable improvement in her status or condition. The patient visibly deteriorated and became untidy, uncooperative, resistive and mute. She refused to eat and was fed by daily gavage. At the insistence of her parents she was again given electroconvulsive therapy on Oct. 21, 1946. It was noted that, possibly due to inanition, her right femoral hernia increased alarmingly with each convulsion. There was some improvement noted during the first three or four treatments, in that the patient began to eat, was less resistive, was much more communicative and was no longer withdrawn and apathetic. This influenced the decision to continue treatment, with the added safeguard of using curare ("intocostrin"). She received six further convulsive treatments with curare premedication, with observable well defined improvement in her status. Following the ninth intravenous administration of curare and subsequent convulsion, respiration ceased. She was given intravenous intramuscular and intracardial injections of neostigmine compound, nikethamide, epinephrine and caffeine, none of which were helpful. Artificial respiration was given for approximately ninety minutes, but normal respiration and cardiac action could not be reestablished and maintained. Postmortem examination failed to reveal anything unusual, and it was felt that this was indeed a death from respiratory paralysis due to treatment with curare. It is to be noted that during the artificial respiration there were periods when the pulse became palpable and, indeed, on two occasions artificial respiration was discontinued because spontaneous breathing took place. On both of these occasions, however, the respiration was short lived.

SUMMARY

The present article is offered in order to present the hazards of curarization prior to electroconvulsive therapy. It is felt that an insufficiency of such reports in the literature tends to make physicians utilizing electroconvulsive therapy less cautious than is warranted with so hazardous a drug as curare. Furthermore, we know too little about the personal sensitivity of patients to this drug. In the case in hand, the patient had tolerated curarization, utilizing the same or greater amounts of curare on five previous occasions without untoward effects. There was no strong indication of the patient's intolerance to curare. Possibly this patient had a subclinical form of myasthenia gravis as described by Riggs and Schlomer.[1] Perhaps other factors were at play, but these could not be adequately determined before the fatal accident.

1. Riggs, B. C., and Schlomer, G. M.: Dis. Nervous. System **8**: 382-38 (Dec.) 1947.

Council on Foods and Nutrition

This paper was prepared at the request of the Council and is one of a series appearing in THE JOURNAL. *Later the entire series will appear in book form as the Council's Handbook of Nutrition.*

JAMES R. WILSON, M.D., *Secretary.*

PROTEINS IN NUTRITION

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The term protein was suggested by the Dutch chemist Mulder in 1839 as a designation for the universal component of tissues, both plant and animal. Protein was characterized by him as "unquestionably the most important of all known substances in the organic kingdom. Without it no life appears possible on our planet. Through its means the chief phenomena of life are produced."[1] Today, more than a century after Mulder, the proteins are still "first" (Greek, *prōteios)* in the regulation of vital processes, and disturbances in their metabolism are associated with nutritive failure and with many pathologic conditions with which the physician is confronted.

Proteins are normal constituents of all animal cells and body fluids with the exception of the bile and the urine. They are essential components of both the protoplasm and the nucleus of the cell; hence they exert a profound influence on growth. They are important in the regulation of osmotic relations between cells and intercellular fluids and between tissues and blood and play a significant role in the fluid balance of the body. Many of the best characterized enzymes have been obtained in crystalline form and have the properties of proteins (the "protein enzymes").[2] A considerable number of the hormones, chemical regulators of the body, either are proteins (the so-called protein hormones)[3] or are derivatives of proteins. Many of the substances associated with immunologic and antigenic reactions and similar phenomena are known to be proteins. In recent years the causative agents of certain virus diseases (notably the tobacco mosaic and the bushy stunt of the tomato) have been obtained in crystalline form and exhibit the characteristic properties of nucleoproteins; yet when inoculated into the proper host they multiply and give rise to the specific pathologic changes associated with the virus.[4] Bacteriophage, a filtrable agent with the properties of a virus, is also believed to be a nucleoprotein. Finally, a nucleoprotein is the major constituent of cell nuclei and is believed to constitute the chromatin of the nucleus and thus to form the principal component of the chromosome.[5]

It is notable that proteins exist as large molecules or, possibly, aggregates of molecules. In table 1 are presented the estimated molecular weights of a few important proteins. It should be pointed out that in the determination of the molecular weights of proteins, many difficult problems arise and that the values obtained by the various methods do not check exactly. The values presented will, it is believed, afford some approximation of the probable size of protein molecules. The large molecules of even the simpler proteins may be compared with those of some other important constituents of tissues or body fluids: sodium chloride, 58; urea, 60; ascorbic acid, 176; dextrose, 180; lactose, 342; carotene (provitamin A), 537, and glyceryl tristearate (a typical fat), 891.

When this large protein molecule is broken down by the addition of the elements of water (hydrolysis), a considerable number of much simpler units, or building stones, are formed, whose molecular weights range from 75 (aminoacetic acid, known also as glycocoll or glycine) to 240 (cystine). These units have the structure and properties of ampholytes (dissociation, so that they may function either as an acid or as a base depending on the p_H of the environment) and are known as α-amino acids. From the chemical standpoint, they are characterized by the presence of a carboxyl (COOH) group with acidic properties and an amino (NH_2) group with basic properties, the two groups being attached to the same carbon atom.

TABLE 1.—*Sources and Approximate Molecular Weights of Proteins*

Protein	Source	Estimated Molecular Weight
Insulin	Pancreas	35,000 or 46,000
Pepsin	Gastric juice	35,200
Bence-Jones protein	Urine	35,200
β-Lactoglobulin	Milk	42,000
Ovalbumin	Hen's egg	43,000
Zein	Corn	50,000
Hemoglobin	Human blood	70,000
Serum albumin	Human blood	70,000
γ-Globulin	Human blood	156,000
Urease	Jack bean	422,000
Thyreoglobulin	Thyroid	650,000
Antipneumococcus serum globul'n	Horse blood	845,000
Bushy stunt virus	Tomato plant	7,600,000
Tobacco mosaic virus	Tobacco plant	40,000,000

The character of the remainder of the amino acid molecule (designated by R, fig. 1) varies, but all the typical products of hydrolysis have in common the presence of the carboxyl and amino groups. Important chemical groupings in various amino acids are sulfur (cystine and methionine), hydroxyl (threonine and serine), benzene nucleus (phenylalanine and tyrosine), guanidine nucleus (arginine), indolyl ring (tryptophan) and imidazolyl ring (histidine).

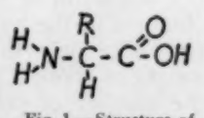

Fig. 1.—Structure of an amino acid.

Certain units or amino acids present in the protein molecule are considered of especial importance in the structure of tissue (growth) and are commonly designated as the essential amino acids. The chemical nature of these essential units will be discussed subsequently. The formulas of the other amino acids may be obtained from any of the numerous standard textbooks on biologic chemistry.

The amino acids are joined to each other in the protein molecule by a linkage known as the peptide linkage, in which the basic (amino) group of one acid is linked to the acidic (carboxyl) group of the adjacent acid.

From the Department of Biological Chemistry, Medical School, University of Michigan.

1. Mulder, G. J.: The Chemistry of Animal and Vegetable Physiology, cited by Mendel, L. B.: Nutrition: The Chemistry of Life, New Haven, Conn., Yale University Press, 1923, p. 16.
2. Northrop, J. J.: Crystalline Enzymes, New York, Columbia University Press, 1939.
3. White, A.: Protein Hormones, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., N. Y., The Biological Laboratory, 1938, vol. 6, p. 262.
4. Stanley, W. M.: Some Chemical, Medical and Philosophical Aspects of Viruses, Science **93**: 145-151 (Feb. 14) 1941.
5. Mirsky, A. E.: Chromosomes and Nucleoproteins, in Nord, F. F., and Werkman, C. H.: Advances in Enzymology and Related Subjects of Biochemistry, New York, Interscience Publishers, Inc., 1943, vol. 3, p. 1. Darlington, C. D.: Nucleic Acid and the Chromosomes, in Symposia of the Society for Experimental Biology, London, Cambridge University Press, 1947, vol. 1, p. 252.
6. Omitted.

with the loss of a molecule of water. A compound made up of two acids thus joined is known as a dipeptide (fig. 2), and a similar compound which contains several (usually an unknown number) amino acids bound together in the peptide linkage is known as a polypeptide.

Hydrolysis of the dipeptide for which the formula is given would break the peptide linkage (-NH-CO-), and the component amino acids would be obtained. While the peptide linkage may not be the only linkage between the amino acids of the protein molecule, it is certainly by far the most important one. This is borne out by the chemical properties of native proteins (proteins as they are found in nature as contrasted with derivatives formed by the action of heat, alcohol, water, salts, enzymes and the like). The biologic reactions of the proteins are also more closely related to those of amino acids than to those of any other type of hydrolytic product of protein, such as proteoses or peptones.

Just like the amino acids, which are ampholytes and may react with either acids or bases, depending on the p_H of their environment, the proteins as complexes of amino acids (polypeptides) may combine with either acids or bases. For the most part, the proteins as they exist in fluids and tissues of the animal organism function as acids (play the role of anions) and are in combination with bases (cations). Thus, the protein hemoglobin of the erythrocytes is combined in the cell with base (chiefly potassium) as a salt; similarly, milk contains various salts of casein, of which calcium caseinate is important.

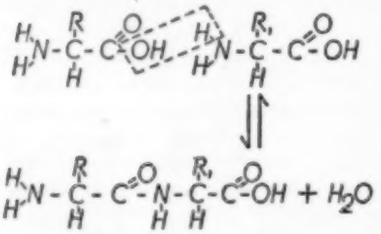

Fig. 2.—Structure of a dipeptide.

When two amino acids are joined in peptide linkage, two different peptides may be obtained; with three amino acids, six peptides, and with five amino acids, 120 peptides. These are known as isomers, since they are all made up of the same units and have the same percentage composition. They differ, however, in the arrangement of the amino acids in the peptide chain (for instance, in the case of a tripeptide, a-b-c, a-c-b, b-a-c, b-c-a, c-a-b and c-b-a, when a, b and c are three different amino acids). Since more than twenty amino acids are known to be of general occurrence in the protein molecule, it is obvious that the possible number of isomeric proteins (polypeptides) is very large. A peptide made up of twenty amino acids, most commonly obtained in the hydrolysis of protein,[7] each acid occurring once only in the chain, would have a molecular weight of about 2,700. A simple calculation shows that the number of possible isomers of this peptide would be 2,432,902,008,176,640,000, a number beyond the range of human thought.[8] Each of these peptides would have the same percentage composition, would yield the same amino acids on hydrolysis in the same proportions and would have similar properties. Each would differ from the other in some slight variation in the arrangement of the component amino acids of the peptide chain. Each would, therefore, be a chemical individual distinct from the other isomeric peptides.

If it is remembered that the protein molecule is much larger than the peptide just discussed, that native proteins vary greatly in the amounts of amino acids which they yield on hydrolysis and that some linkages other than the simple peptide linkage almost certainly occur in the protein molecule, it is evident that the possible number of different proteins as they exist in nature is almost infinite. This individuality of natural proteins finds expression in the so-called specificity of the proteins. This may be most simply defined by the statement that every species tends to construct within the organism a protein characteristic of that species. Thus, casein of cow's milk is believed to differ from casein of goat's milk, protein of beef muscle to differ from protein of pork muscle and serum protein of human blood to be different from serum protein of beef blood. While in my opinion the basis of this specificity is undoubtedly chemical and is related to the possibilities of isomerism just discussed, this cannot be proved at present. The specificity of proteins of different biologic origin must for the present be demonstrated by biologic reactions, by the reactions observed when "foreign" protein is introduced into the organism. The phenomena of anaphylaxis, of antibody formation, of food allergies and of many other antigenic and immunologic reactions are all manifestations of this biologic specificity of the proteins, so important in many considerations of medical practice.

The protein of the human diet is obtained from both animal and vegetable sources. Among foodstuffs of animal origin, meats (both muscular and glandular tissues), fish, eggs, milk and milk products are most important. Vegetable protein is most readily available in the cereal grains (wheat, corn, rice, rye and barley), the seeds of legumes (peas and various kinds of beans) and many nuts, of which the peanut is perhaps most important in the human diet. It is estimated that the cereals contribute about 25 per cent of the total calories of the diet of the American people.

The proteins of the foodstuffs, large molecules with colloidal properties, do not diffuse readily through biologic membranes. If these dietary proteins are to be utilized, it is necessary that they be altered so that passage through the mucous membrane of the intestine is possible. This is accomplished in the gastrointestinal canal by the process of digestion, by the action of a group of biologic catalysts or enzymes, whose activities are so coordinated as to effect a rapid and complete hydrolysis to the soluble diffusible amino acids. Since biologically the amino acids are nonspecific, digestion results in the loss of the biologic specificity of the proteins; if this were not the case, large amounts of "foreign" protein would normally enter the blood stream from the alimentary canal and food allergies of protein origin would be of frequent occurrence.

The enzymes concerned in this process are pepsin and rennin of the gastric juice, trypsin and chymotrypsin of the pancreatic juice and a group of enzymes known as peptidases, which are present in the pancreatic and intestinal juices and hydrolyze the peptides. (It should be noted that commercial "trypsin" and the trypsin referred to in the older literature are mixtures of the proteolytic enzymes of pancreatic tissue and include not only trypsin but also chymotrypsin and peptidases.[9]) Digestion is best effected if these enzymes act on the proteins of the diet in the natural anatomic sequence, i.e., gastric, pancreatic and intestinal.

7. Two amino acids commonly listed in textbooks of biochemistry are not now accepted as units of the protein molecule, i. e., hydroxyglutamic acid and norleucine.

8. Abderhalden, E.: Lehrbuch der physiologischen Chemie, ed. 6, Berlin, Urban & Schwarzenberg, 1931, p. 302.

9. Northrop,[3] pp. 62-63.

Digestion proceeds rapidly in the intestine; the amino acids are absorbed as rapidly as they are formed by the activity of the enzymes. Although digestion studies in vivo with experimental animals with fistulas at various levels throughout the alimentary canal have clearly demonstrated that the major portion of the ingested protein is completely hydrolyzed to amino acids, or at least to very simple peptides,[10] the question of the absorption of some portion of the protein of the diet in unaltered form into the circulation must be considered. Early workers whose experimental methods were not adequate were led to favor the possibility of such an absorption in unusual circumstances, particularly in young animals, in which the intestinal membrane was assumed to be more readily permeable. The use of the newer methods of immunology, by which accurate detection and differentiation of very small amounts of specific proteins have been made possible, has thrown new light on the question. By these methods it now appears to have been demonstrated that in many persons, without regard to age or sex, a detectable amount of certain proteins frequently enters the blood stream in an unaltered state via the alimentary canal. As Walzer [11] has expressed it, "The regularity with which the phenomenon occurs in the average individual and the uniformity of results when repeatedly tried under identical conditions on the same subject, preclude the possibility that this is an accidental or unusual occurrence." Of the protein foods studied, the most extensive observations have been reported with egg white.[12] These observations are of special significance in relation to the phenomena of sensitization to specific protein foods. However, it should be remembered that the methods of immunology are capable of detecting exceedingly minute amounts of protein and that the total amount of protein absorbed thus unaltered must be slight. One may, then, with a reasonable degree of confidence look to the behavior of the individual amino acids for the interpretation of the role of protein in normal nutrition.

The products of the digestion of proteins, chiefly the amino acids, enter the portal blood on absorption from the intestine and are distributed to the tissues by the systemic blood. The postabsorptive increase in the amino acid nitrogen of the blood, although not large, is unquestioned. The amino acids are rapidly taken up by the tissues, and the amino acid content of the blood returns to normal.[13]

One of three fates awaits the amino acids which thus enter the cell. The first is condensation with other amino acids, selected by the particular tissue in question from the pabulum supplied to it by the blood, to form the protein characteristic of that particular tissue or cell. This specific synthesis, the converse of digestion, makes possible the maintenance of the individuality of the cell. This process acquires a particular significance in young animals in which building of new tissues, growth, must occur for normal development and in the adult in normal pregnancy and lactation.

A second metabolic path is utilization of the amino acids for some special purpose in the animal economy apart from the general synthesis of cellular protein. Examples of this are the synthesis of such proteins as hemoglobin, fibrinogen and the serum proteins. Amino acids are utilized also for the formation of specific proteins with hormonal function (insulin and prolactin) or amino acid derivatives which are hormones (epinephrine and thyroxine) or chemical regulators which are not usually classed as hormones (glutathione, histamine and creatine). The synthesis of the "protein enzymes" (pepsin, trypsin, catalase and carbonic anhydrase) also occurs. The details of the reactions which lead to the synthesis of such specialized proteins and protein derivatives are not as yet clearly understood.

After the needs of the cells for these two purposes have been met, an excess of amino acids may still remain in the cells. The fate of this amino acid fraction is deamination—removal of the nitrogenous portion of the molecule—and utilization of the non-nitrogenous portion, since, in contrast to fat and carbohydrate, storage of protein or amino acids for any considerable time does not appear to be possible. The nitrogenous fraction of the molecule, split off as ammonia, is rapidly converted into urea under normal conditions and is eliminated in this form by the kidneys. The efficiency of this transformation is demonstrated by the fact that normally systemic blood contains less than 0.1 mg. of ammonia nitrogen per hundred cubic centimeters, while the urea content of normal blood calculated as urea nitrogen is approximately 17 mg. per hundred cubic centimeters. The non-nitrogenous residue which remains after deamination may either be transformed into dextrose and used in this form, the antiketogenic fraction of the protein molecule, or be converted to fatty acids, the ketogenic fraction of the protein molecule. Whether the non-nitrogenous residue is converted to dextrose for utilization in that form depends on the chemical structure of the original amino acid. In general, one may say that about half of the amino acids present in the molecule of any individual protein may give rise to dextrose in intermediary metabolism.

Physiologic and nutritional studies alike have emphasized the role of the amino acids as structural elements, the building stones of living protoplasm. What are the amino acid requirements for the construction of new cells? Are all the amino acids of equal importance in nutrition? These questions have been answered in part by the studies of Rose, which were based on the pioneer work of Hopkins and of Osborne and Mendel. It should be emphasized that the discussion immediately following concerns the requirements for growth of one species, the white rat. Rose [14] first demonstrated that it was possible to obtain normal growth of young white rats when the protein element of the diet was supplied by a mixture of chemically pure amino acids, which included those acids known to be of general occurrence in the protein molecule. The effect of the removal of the various individual amino acids from this mixture was then studied. The absence of certain acids from the diet resulted in impaired growth or in some cases considerable losses in weight and ultimately death. These amino acids, designated

10. Abderhalden, E.; Kautzsch, K., and London, E. S.: Studien über die normale Verdauung der Eiweisskörper im Magendarmkanal des Hundes, Ztschr. f. physiol. Chem. **48**: 549-556, 1906. Abderhalden, E.; Baumann, L., and London, E. S.: Weitere Studien über die normale Verdauung der Eiweisskörper im Magendarmkanal des Hundes, ibid. **51**: 384-390, 1907.

11. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings: I. A Simple Direct Method of Studying the Absorption of Undigested Protein, J. Immunol. **14**: 143-174 (Sept.) 1927.

12. Wilson, S. J., and Walzer, M.: Absorption of Undigested Proteins in Human Beings: IV. Absorption of Unaltered Egg Proteins in Infants and Children, Am. J. Dis. Child. **50**: 49-54 (July) 1935. Ratner, B., and Gruehl, H. L.: Passage of Native Proteins Through the Normal Gastrointestinal Wall, J. Clin. Investigation **13**: 517-532 (July) 1934.

13. Van Slyke, D. D.: Physiology of the Amino Acids, Science **95**: 259-263 (March 13) 1942.

14. Rose, W. C.: The Significance of the Amino Acids in Nutrition, in Harvey Lectures, 1934-1935, Baltimore, Williams & Wilkins Company, 1936, vol. 30, p. 49; The Physiology of Amino Acid Metabolism, Proc. Inst. Med. Chicago **12**: 98-110 (April 15) 1938.

as essential, could not be synthesized by the rat and had to be supplied in the diet in adequate amounts or nutritive failure resulted. The withdrawal of other amino acids did not influence the rate of growth. These amino acids, the nonessential amino acids, must, therefore, be synthesized in the body at a speed commensurate with the needs for normal growth. In table 2 is presented Rose's listing of the amino acids on this basis. In further studies in which rats have been fed a mixture of the ten essential amino acids listed with the omission of all the nonessential acids, this mixture of amino acids in suitable proportions has been observed to be a "remarkably efficient source of nitrogen for many physiologic functions." [15] On such mixtures, rats not only grew satisfactorily but were able to reproduce and rear their young, which is evidence of effective lactation. In the group of essential amino acids, arginine occupies a unique position. Growth is possible in the absence of this amino acid from the diet, but the rate of growth is distinctly less than when arginine is supplied.* Rose has defined an indispensable dietary component as "one which cannot be synthesized by the animal organism, out of the materials ordinarily available at a speed commensurate with the demands for normal growth." [16]. If this definition is accepted, arginine is classed as essential. This classification of amino acids is one based on the growth requirements of rats. Whether modifications must be made when requirements for pregnancy, lactation or maintenance are under consideration remains to be determined.

TABLE 2.—*The Amino Acids Essential for Growth of the White Rat*

Amino Acid	Characteristic Chemical Grouping
Threonine	Hydroxy group on 4 carbon chain
Valine	5 carbon branched chain
Leucine	6 carbon branched chain
Isoleucine	6 carbon branched chain
Lysine	2 amino groups on 6 carbon chain
Tryptophan	Indole nucleus
Phenylalanine	Benzene nucleus
Methionine	Methyl thiol group
Histidine	Imidazole nucleus
Arginine*	Guanido group

* Arginine has a special position, as discussed in the text.

The possibility of species differences must also be considered. It is known that all of the amino acids essential for the young white rat are also essential for the growth of the young chick.[17] The amino acids required for maintenance of nitrogen balance in young adult humans has been studied by Rose [15] and Holt.[18] According to Rose, all of the amino acids essential for the growth of the young white rat, except histidine and arginine, are necessary as dietary constituents, if nitrogen balance is to be maintained in human adults. When any one of the eight essential amino acids was excluded from the food, there resulted a "pronounced negative nitrogen balance, a profound failure in appetite, a sensation of extreme fatigue, and a marked increase in nervous irritability. These symptoms were observed even when the subjects were unaware that a dietary alteration had been made. With the return of the missing amino acid to the food, nitrogen equilibrium was reestablished promptly, and the subjective symptoms disappeared." [15a] Histidine and arginine, on the other hand, were not necessary for the maintenance of nitrogen equilibrium in the human adult.

Rose [15a] has gone further and has attempted to estimate the upper limits of the daily requirements of the essential amino acid in human beings under the previously outlined conditions. These values (table 3) represent the highest possible requirements of a man weighing 70 Kg. and "may be, and probably are, higher than the minimum requirement." It will be noted that the weight of the amino acids represented in the table totals slightly over 30 Gm. Full details of these experiments will be awaited with much interest.

In the experiments of Holt [18] with young men, an interesting observation was the decrease in the number of spermatazoa in the seminal plasma when arginine was removed from the diet and the return to normal counts when arginine was restored to the diet. These experiments must be confirmed and extended before practical applications in the clinical treatment of sterility in men are attempted. It is known that the testicular tissue of fish has a high content of arginine, but, so far as is known to me, no analysis for arginine has been made with human spermatazoa nor have similar analyses of other mammalian sperm been available. Recently, however, analysis of bovine sperm has revealed a high arginine content (25.47 per cent on a fat-free, moisture-free and ash-free basis).[19]

It is assumed that the amino acids not listed in table 2 are dispensable and, if absent from the diet, can be synthesized. Womack and Rose have discussed the interrelationships of arginine, proline and glutamic acid in the diet.[20] Glutamic acid is tentatively listed as nonessential for growth of the young white rat.

The tissue protein synthesized during growth in such experiments must be assumed to be of a type normal and characteristic of the species, since it is considered axiomatic that "the tissues either form a typical protoplasmic product, or none at all." [21] In the case of the sulfur-containing amino acids, the evidence seems clear that the dispensable cystine may be synthesized from the essential methionine.[22]

TABLE 3.—*Upper Limits of the Daily Requirements*

	Per Kilogram of Body Weight (Mg.)	For a Man Weighing 70 Kg. (Gm.)
Valine	59	4.13
Leucine	67	4.69
Isoleucine	42	2.94
Threonine	42	2.94
Methionine	50	3.50
Phenylalanine	59	4.13
Tryptophan	26	1.82
Lysine	84	5.88

The function of the essential amino acids, other than for the construction of new protoplasm, is not entirely

15. (*a*) Rose, W. C.: Role of the Amino Acids in Human Nutrition, Proc. Am. Philos. Soc. **91**: 112-116 (Feb.) 1947. (*b*) Harte, R. A., and Travers, J. J.: Human Amino Acid Requirements, Science **105**: 15-16 (Jan. 3) 1947.

16. Rose, W. C.: The Nutritive Significance of the Amino Acids, Physiol. Rev. **18**: 109-136 (Jan.) 1938.

17. Almquist, H. J.: Evaluation of Amino Acid Requirements by Observations on the Chick, J. Nutrition **34**: 543-563 (Nov.) 1947.

18. Holt, L. E., Jr.: Amino Acid Deficiencies in Man in Nutrition and Public Health in the Postwar Period, Detroit, Children's Fund of Michigan, 1944, p. 193.

19. Sarkar, B. C. R.; Luecke, R. W., and Duncan, C. W.: The Amino Acid composition of Bovine Sperm, J. Biol. Chem. **71**: 463-465 (Dec.) 1947.

20. Womack, M., and Rose, W. C.: The Role of Proline, Hydroxyproline, and Glutamic Acid in the Diet, J. Biol. Chem. **171**: 37-50 (Nov.) 1947.

21. Osborne, T. B., and Mendel, L. B.: Amino Acids in Nutrition and Growth, J. Biol. Chem. **17**: 325-349, 1914.

22. Lewis, H. B.: The Significance of the Sulfur-Containing Amino Acids in Metabolism, in Harvey Lectures, 1940-1941, Baltimore, Williams & Wilkins Company, 1942, vol. 36, p. 159. Rose, W. C., and Wood, T. R.: The Synthesis of Cystine in Vivo, J. Biol. Chem. **141**: 381-389 (Nov.) 1941.

clear. Methionine is a precursor of cystine, an amino acid important in the molecule of the proteins of epidermal structures and also of certain hormones, particularly insulin, in the molecule of which 12 per cent of cystine is present and no methionine.[23] Methionine also supplies methyl groups for the synthesis of choline, a dietary essential, and of creatine, important for maintenance of muscle function.[24] Phenylalanine presumably furnishes the nucleus for the synthesis of thyroxine, the iodine-containing amino acid present in the specialized physiologically active thyroglobulin of the thyroid, and of epinephrine, the endocrine principle of the adrenal medulla.[25] Histidine may be decarboxylated to yield histamine, the amine whose biologic role seems demonstrated.[26] Arginine is believed to supply the amidine group for the synthesis of creatine.[27] Specific functions for the other essential amino acids are yet to be suggested. It is also of interest to note that the essential amino acids comprise slightly more than half of the amino acid rests of β-lactoglobulin, one of the best characterized purified proteins.[28]

An interesting recent development has been relationships between vitamins and amino acids. It was observed that in rats fed certain types of low protein diets retarded growth resulted, a retardation which could be corrected by the addition of either nicotinic acid or tryptophan to the diet. This suggested that tryptophan might function as a biologic precursor of nicotinic acid.[29] When rats or mice were fed diets deficient in pyridoxine, an abnormal chromogenic substance, xanthurenic acid, which was shown to be a derivative of tryptophan, was excreted in the urine.[30] Administration of tryptophan increased the excretion of xanthurenic acid. The full significance of these studies is not clear, but it appears probable that study may reveal more such relationships between proteins (amino acids) and the various vitamins.[31]

For the proper utilization of the observations concerning the essential and nonessential amino acids and their role in the diet, more complete information is needed concerning the amino acid composition of important food stuffs on which our supply of dietary protein depends. The nutritive value of important protein foods can then be evaluated. Some data of this type, in which the newer microbiologic methods are used as well as chemical methods, are now available.[32] An important application of the observations that properly chosen mixtures of amino acids may replace proteins in nutrition has been the clinical use of protein hydrolysates, prepared for the most part by enzymatic action on proteins in vitro. These preparations may be administered either orally or parenterally. The utilization of intravenously injected amino acids over a considerable period was first demonstrated by Henriques and Anderson[33] in experiments with a goat.

The clinical use of such protein hydrolysates has been studied extensively by Elman[34] and others.[35] Intravenous administration of protein hydrolysates has been shown to be beneficial when feeding by mouth is not possible or is inadvisable. Since hydrolysis destroys the biologic specificity of the native proteins, protein hydrolysates orally administered have proved of value in supplying nitrogen to persons with severe food allergies. Whipple and his co-workers have demonstrated that protein hydrolysates may function effectively in the restoration of plasma protein in dogs in which reserve of tissue and plasma proteins have been depleted by bleeding.[35d] More extensive clinical studies of the usefulness of protein hydrolysates in medical and surgical patients are desirable.

The problem of the amount of protein which is essential or optimal in the diet of human beings has received much attention. The optimal protein level is particularly important in view of the higher cost of protein foodstuffs, notably meat, which makes it of doubtful economy to use protein primarily for energy purposes. Stare[36] recently stated that, for the production of 1,000,000 human food calories derived from cane sugar, 0.15 acre of land is required; this is in sharp contrast to 17 acres, the acreage required to produce the same amount of energy from steers.

It is usually accepted that luxus consumption of protein over prolonged periods is of no permanent value to the adult organism, since, in contrast to fat and carbohydrate, protein and its building stones, the amino acids, are not stored.[37] This is seen in the state of nitrogenous equilibrium or balance. If the dietary protein of a normal adult is adequate, the nitrogen of the diet (chiefly protein nitrogen) is equal to the nitrogen of the excreta (mainly the nitrogen of the urine). If to the diet of such a person increased amounts of protein are added, there is a sharp increase in the nitrogenous waste products of the urine (largely urea, derived from protein catabolism), and within a relatively short time nitrog-

23. Miller, G. L., and du Vigneaud, V.: The Cystine Content of Insulin, J. Biol. Chem. **118:** 101-110 (March) 1937. du Vigneaud, V.; Miller, G. L., and Rodden, C. J.: On the Question of the Presence of Methionine in Insulin, ibid. **131:** 631-640 (Dec.) 1939.

24. du Vigneaud, V.: The Significance of Labile Methyl Groups in the Diet and Their Relation to Transmethylation, in Harvey Lectures, 1942-1943, Baltimore, Williams & Wilkins Company, 1944, vol. 38, p. 39. Lewis.[22]

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26. Best, C. H., and McHenry, E. W.: Histamine, Physiol. Rev. **11:** 371-477 (Oct.) 1931.

27. Bloch, K., and Schoenheimer, R.: The Biological Precursors of Creatinine, J. Biol. Chem. **138:** 167-194 (March) 1941.

28. Brand, E.; Saidel, L. J.; Goldwater, W. H.; Kassell, B., and Ryan, F. J.: The Empirical Formula of β-Lactoglobulin, J. Am. Chem. Soc. **67:** 1524-1532 (Sept.) 1945.

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30. Lepkovsky, S.; Roboz, E., and Haagen-Smit, A. J.: Xanthurenic Acid and Its Role in the Tryptophane Metabolism of Pyridoxine-Deficient Rats, J. Biol. Chem. **149:** 195-201 (July) 1943. Miller, E. C., and Baumann, C. A.: Relative Effects of Casein and Tryptophane on the Health and Xanthurenic Acid Excretion of Pyridoxine-Deficient Mice, ibid. **157:** 551-562 (Feb.) 1945.

31. Mitchell, H. H.: The Chemical and Physiological Relationships Between Vitamins and Amino Acids, in Harris, R. S., and Thimann, K. V.: Vitamins & Hormones, New York, Academic Press, Inc., 1943, vol. 1, pp. 157-194.

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33. Henriques, V., and Anderson, A. C.: Ueber parenterale Ernahrung durch intravenose Injektion, Ztschr. f. physiol. Chem. **88:** 357-369, 1913.

34. Elman, R.: Parenteral Alimentation in Surgery with Especial Reference to Proteins and Amino Acids, New York, Paul B. Hoeber, Inc., 1947.

35. (*a*) Allison, J. B.; Anderson, J. A., and Seeley, R. D.: The Determination of the Nitrogen Balance Index in Normal and Hypoproteinemic Dogs, Ann. New York Acad. Sc. **47:** 245-271 (Oct. 30) 1946. (*b*) Barnes, H., and Bosshardt, D. K.: The Evaluation of Protein Quality in the Normal Animal, ibid. **47:** 273-296 (Oct. 30) 1946. (*c*) Chow, B. F.: The Electrophoretic Studies on the Effect of Protein Depletion on Plasma Proteins and the Regeneration of Plasma Proteins After Oral Administration of Hydrolysates Prepared from Casein and Lactabumin, ibid. **47:** 297-316 (Oct. 30) 1946. (*d*) Whipple, G. H.; Robscheit-Robbins, F. S., and Miller, L. L.: Blood Protein Regeneration and Interrelation, ibid. 317-326. (*e*) Peters, J. P.: Nitrogen Metabolism in Acute and Chronic Disease, ibid. **47:** 327-345 (Oct. 30) 1946. (*f*) Elman, R.: The Intravenous Use of Protein and Protein Hydrolysates, ibid. **47:** 345-357 (Oct. 30) 1946. (*g*) Co Tui: Clinical Experience with Oral Use of Protein Hydrolysates, ibid. **47:** 359-373 (Oct. 30) 1946. (*h*) Cannon, P. R.: Amino Acid Utilization in the Surgical Patient, J. A. M. A. **135:** 1043-1046 (Dec. 20) 1947.

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37. Kosterlitz, H. W.: The Storage of Protein in the Adult Animal, Nutrition Abstr. & Rev. **15:** 1-14 (July) 1945.

enous equilibrium is again obtained, but at a higher level of excretion. If new protein is being synthesized in the body (growth, pregnancy and lactation), the nitrogen excreted is less than that of the diet and the subject is said to be in positive nitrogen balance. When the nitrogen excreted is greater than the dietary nitrogen, a condition of negative balance is obtained. This indicates an inadequate intake of dietary protein or an excessive breakdown of body protein associated with disease.

The level of endogenous nitrogen protein metabolism may be obtained by a consideration of the nitrogen excretion of an adult maintained on a diet high in its content of fat and carbohydrate but containing no protein. Experimentally this has been observed to approximate 3 Gm. a day for a man weighing 70 Kg., or about 20 Gm. of protein.[38] There is, however, evidence that to provide a safe allowance for health, protein in excess of the requirements for maintenance is essential. It is argued that excessive consumption of protein imposes a burden on the organism and is likely to be harmful. The proponents of the high protein diet, on the other hand, argue that a surplus of protein may have a beneficial effect on health and well-being and cite studies of racial groups which indicate that physical efficiency and health can be related directly to the intake of protein and particularly of animal protein. The high protein diet of the Eskimo, in which the protein is obtained almost entirely from meat, does not appear to have resulted in a high incidence of renal disease in this group.[39] The carefully made studies of the metabolism of two Arctic explorers who lived for a year in the temperate zone on a diet of meat only are of particular interest. It must be remembered, however, that in studies of human populations the protein element is only one of many factors in health and that it is difficult to assess the role of dietary protein alone without many greatly extended studies.[40]

Outstanding among the pathologic conditions which have been associated with prolonged ingestion of a diet inadequate in its protein content is nutritional edema (known also as war or starvation edema), which has been observed clinically in Europe, in the Orient and in the United States and can be produced experimentally in animals maintained on a low protein diet.[41] The continued ingestion of the low protein diet results in low levels of plasma protein (particularly the albumin fraction), and the resultant lowering of the "effective" osmotic pressure of the plasma is believed to be one of the causes of the edema.

This discussion indicates the desirability of caution in the selection of a standard protein level for national nutrition. It is not necessary to enter into the details of the controversy between the advocates of the low and high protein diet, a controversy which is excellently and impartially presented in the classic text of Lusk.[42] Sherman, after a careful consideration of the acceptable balance experiments with human beings, in which nitrogen equilibrium was established at low levels of dietary protein, concluded that "a standard allowance of 1 Gm. of protein per kilo of body weight per day appears, therefore, to provide a margin of safety of 50 to 100 per cent as far as requirements of adult maintenance are concerned."[43] This standard for adult maintenance has been accepted almost universally, while the need for larger amounts of protein in diets of growing children and of pregnant and lactating women is clearly recognized. The recently adopted standards for national nutrition, as proposed by the Food and Nutrition Board of the National Research Council, provide for 70 Gm. of protein a day in the diet of a man weighing 70 Kg. and 60 Gm. of dietary protein for a woman weighing 56 Kg.[44]

Estimates of the increased requirements for protein during pregnancy and lactation vary greatly.[45] The protein requirement per kilogram of body weight is high in infancy and decreases as growth occurs until after puberty, when the adult requirements only are necessary. The desirable amount of dietary protein is estimated to vary from 4 Gm. per kilogram a day at 1 to 3 years to 2 Gm. at 17 to 18 years.[44] The necessity of proteins of milk, during the period of active growth can hardly be overemphasized. That increased muscular activity necessitates a larger intake of protein is as yet unproved. Traditionally the diet of highly trained athletes and of laborers engaged in hard work, whose calorific requirements are high, contains much meat and supplies large amounts of proteins.[40]

An increased destruction of tissue protein has long been recognized in a variety of infectious diseases. More recently, loss of nitrogen, as evidenced by decided negative balances, has been observed in patients undergoing surgical treatment (notably after fractures) and in patients with severe burns.[46] In an attempt to make good this loss of protein from the body, a loss which may continue for some days, high protein diets have been recommended, which supply quantities of protein far in excess of those of the "recommended dietary allowances" of the Food and Nutrition Board.[44] The cause of this increased destruction of protein is not yet understood.[47]

The preceding discussion has been concerned with the quantitative aspects of the protein requirements of human beings. That the dietary protein will be derived from a wide variety of foodstuffs of both animal and vegetable origin is assumed. In the United States, it is estimated that animal protein makes up at least 50 per cent of the protein of the usual diet. If the variety of foodstuffs is limited, care must be exercised in the selection of protein. The chief consideration in the choice of protein must be the furnishing of the essential amino acids to be made available to the tissues by digestion. Since the optimal mixture of the essential amino acids for the nutrition of human beings is not yet known, the diet must supply all the known essential amino acids in liberal amounts. Animal proteins usually have a greater biologic value than do the proteins of vegetable origin. Thus zein, one of the proteins of

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the maize kernel, contains no lysine or tryptophan, two important essential amino acids. When the diet is derived exclusively from plant materials, more protein must be eaten. A notable exception is gelatin. This protein, a product of food technology and derived from collagen, completely lacks at least two essential amino acids, valine and tryptophan, and contains little tyrosine and cystine, amino acids which, while not essential, may be important in nutrition. Gelatin supplies a mixture of amino acids, which is inadequate if used as the sole or chief source of these tissue-building stones. The recent claims for the superior food value of gelatin require further and more careful study.[48] The excellent quality of the mixture of proteins present in milk is notable.

Carbohydrates spare body protein. The breakdown of body protein is significantly increased if the supply of the energy-producing foods and particularly of carbohydrates is not ample. The consideration of the total calorific value of the diet is of special importance when the diet is low in its protein content, as are certain diets prescribed for therapeutic purposes. Diets of high calorific content usually contain liberal or large amounts of protein.

It is known that in the case of certain essential elements present in food (notably the vitamins) the nutritive value may be influenced by preservation, processing and cooking. Thus the nutritive values of a natural foodstuff as determined by chemical analysis may not be a safe guide to its value when prepared for consumption. Since foodstuffs which are important sources of protein are seldom consumed in the raw state, possible changes due to heat must be considered. Even milk in present day practice is usually subjected to the mild heat of pasteurization. The evidence in the case of proteins is conflicting. The biologic value of the protein of certain legumes is believed to be increased by cooking, while the nutritive value of some other proteins (meat, casein and milk products) appears to be lowered by heat.[49] A detailed discussion is not possible here. Whether such changes are sufficiently extensive to be of practical significance remains to be determined.

No discussion of recent developments in protein metabolism can neglect the mention of the experiments of Schoenheimer in which isotopic nitrogen (N^{15}) has been used as a marker.[50] These experiments indicate that a "rapid and continuous chemical regeneration of the cell proteins is a general characteristic of living matter," but, despite this striking and continuous chemical activity of the organ proteins, it is believed that these processes "lead to no final quantitative or qualitative changes" in the composition of the tissues.[51] This is in confirmation of the older belief in the constancy of composition of the structural elements of protoplasm. While the observations of Schoenheimer and his group are of great physiologic significance, it is not believed that at present they suggest any changes in the current practices of dietetics so far as concerns protein.

In an earlier discussion (1942) of protein in nutrition, I quoted Karl Thomas (1929), with reference to the chief unsolved problems of the role of proteins in nutrition. No better conclusion to this presentation of the problems of 1948 can be given than to reiterate the statements of Thomas.[52] "What we need to know is: 1. Which amino acids must be present in the food, 2. How much we require of each, 3. And to what purpose." Today, after more than a decade of intense interest and research in protein metabolism, these questions still epitomize the problem of the role of proteins in nutrition. When they can be answered exactly, the role of protein in the diet will be known and one will be able to determine the dietary value of every mixture of proteins in natural foodstuffs. Until this knowledge is obtained, one may rest assured that for the healthy person, natural protein chosen from a wide variety of foodstuffs and supplied in ample amounts is the practical solution of the problem of dietary protein. The body may be able to synthesize the nonessential amino acids from the essential ones, but there is no knowledge that the imposition of this task on the cells represents physiologic economy. Living organisms have synthesized a wide variety of proteins containing both essential and nonessential amino acids; surely one cannot do better at present than to insure such a supply of amino acids as mixed proteins afford. The gastronomic urge will prompt one to eat meat, eggs and other protein foodstuffs in preference to unappetizing protein hydrolysates or mixtures of pure amino acids.

SUMMARY

Proteins are large complex molecules with colloidal properties and function as ampholytes, i.e., may dissociate, either as acids or bases. The structural units of the protein molecule are α-amino acids, of which some nineteen are clearly recognized as components of the usual types of proteins.

Proteins are almost completely digested to the amino acids in the gastrointestinal canal; the amino acids are absorbed into the portal blood and circulate in the systemic blood, from which they are rapidly removed and stored for use by the cells of the various tissues.

The amino acids, thus made available from the diet, may be used for the various synthetic reactions, formation of proteins and of essential products derived from amino acids (e.g., thyroxine, epinephrine). The amino acids not required for synthesis are deaminized with oxidation to yield ammonia and α-keto acids. The ammonia is converted to urea and excreted by the kidneys.

Certain amino acids, designated as essential, cannot be synthesized by the mammalian organism and must be supplied by the diet. The other, nonessential, amino acids can be synthesized by the body.

Both animal and vegetable foodstuffs are good sources of protein, provided that they supply adequate amounts of the essential amino acids. In the usual American dietary, the amounts of protein derived from animal (meats, fish, milk and milk products, eggs) and vegetable (cereals, legumes, nuts) sources are about equal.

The minimal recommended protein of the diet for an adult man (70 Kg.) is 70 Gm., or 1 Gm. per kilogram of body weight, and for an adult woman 60 Gm. The required amounts of dietary proteins are increased by pregnancy and lactation. The requirements of the growing child are greatly in excess of those of the adult (e.g., 2 to 4 Gm. per kilogram of body weight per day).

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SATURDAY, SEPTEMBER 18, 1948

THE HAZARDS OF X-RAY

Medical science advances rapidly. New discoveries are announced frequently. This makes the physician's responsibility heavier and heavier. He has to know the old science and the new also. He has to know the power and the hazards of new devices and must use good judgment in balancing probable good against possible harm.

Think of radiation! The engineers and the nuclear physicists keep developing new apparatus. New researches, including some by the health physicists and biologists connected with the development of the atom bomb, have taught us more about the hazards of the old apparatus, also, such as x-ray and radium.

Even small quantities of roentgen or radium rays can prove damaging. Radiation injury to the skin sometimes leads to cancer, coming even many years after. Some of these patients did not show immediate injury, even so much as redness of the skin. Repeated or continuous irradiation of the whole body can produce aplastic anemia, sometimes leukemia, even when the individual doses have been moderate.

Roentgen rays for diagnosis (films and fluoroscopy) are safe only because radiologists have a long tradition of being careful and because films and screens are so sensitive as to require rather small exposures. Examples of accidental erythema or redness continue to appear, and even of disastrous roentgen ulceration. Many of these come from fluoroscopy for bone setting and for removing foreign bodies. The hazard seems higher among surgeons and general practitioners than among x-ray specialists. Paradoxically, the smaller types of x-ray machines have provided most of the worst cases. Every radiologist has a collection of anecdotes to show how dangerous roentgen rays can be in the hands of those not specially trained.

In treating cancer big doses of radiation are used. Resulting damage to skin and normal structures is severe and obvious. Blistering is often only the proof that a thoughtful and conscientious therapist has given enough radiation to have a chance to cure. Such damage, including the possibility of late roentgen ulceration, or late roentgen cancer, is not too high a price to pay for cure of a cancer; regrettable, but at present necessary. Perhaps new medical discoveries regarding cancer will outmode the present radiation therapy.

Until then physicians will continue to apply radiation. Patients will bear the accompanying damage. Radiologists must continually test and retest their judgment to see that it is dependable in applying such doses, and they must measure and remeasure the critical quantities of roentgen rays that are applied.

When benign conditions, not cancer and not lethal, are concerned the point of view is different. The situation is not desperate. If the disease does not threaten life, treatment that may do harm should be avoided, or treatment that may lead to trouble later in life. Are radiologists too light hearted in advising a few hundred roentgens for subacromial bursitis? What degree of desperation should be demanded in this painful condition before inflicting the (rather mild) roentgen injury incidental to 300 r? And if not relieved, how many times shall the damage be compounded by repeated dosage? There is no "official" answer to this or to similar pointed questions in the therapy of acute and chronic arthritis. Such a dose may in fact be thoughtfully accepted in many a case, but in every instance it ought assuredly to be thoughtful and not "routine."

In cases of postoperative parotitis or of gas gangrene, such moderate doses are given more boldly, even though one is less sure of their effectiveness, for the acute danger of the disease is apparent.

In dermatitis, especially allergic dermatitis, roentgen radiation is often an almost magical palliative. Recurrences are common. Treating the recurrence increases the total irradiation. After many recurrences the total mounts to the danger limit, but one also foresees that the patient will have been well persuaded by the many temporary successes that roentgen irradiation is the treatment he needs. His demand for another treatment may be well nigh undeniable. Foresight therefore warns that one should not use roentgen rays in dermatitis until literally everything else has been tried most patiently.

Many babies have red birthmarks, hemangiomas, typically "strawberry marks." These often respond well to roentgen rays or radium. Heavy doses have been followed in some by equally unsightly scars or telangiectases. A few have resulted in arrest of epiphysial growth and a deformed limb. There are reports that nearly all strawberry marks disappear spontaneously by the age of 5 years. In the face of this, a radiologist needs to be sure indeed that his irradiation is such as will do little damage to the skin and no damage to the bones.

Common warts are distressing to fastidious persons and on the sole of the foot can be crippling. Topical, surgical and medicinal treatments are often disappointing. Radiologists rather generally accede to a request to treat them, and many times succeed. Doses advised are not small in amount, and are tolerable at all only because small in area. Nevertheless, there are many instances of ulcers following roentgen irradiation even by trained radiologists. Perhaps it is too soon to condemn such therapy, but at least the treatment should not be undertaken lightly. One should be certain of the dose and area. Careless history taking or slovenly records can result in repeated irradiation of the same area. This can be disastrous, even if the interval between treatments has been long.

In attempts to stem the discouraging tide of hardness of hearing great enthusiasm has developed for radium irradiation of the mouth of the eustachian tube. This is being applied to children under the supposition that much adult deafness arises from years of interference with aeration of the tympanum. How good the statistical evidence is of this etiology of adult deafness is not yet established. One has no doubt of the effectiveness of irradiation in shrinking the hypertrophied lymphoid tissue. The real question, not yet answered, is how much late damage may develop from these irradiations. Although the total dose in milligram-hours seems small (1 per cent of what is often used in uterine cancer), yet the local tissue dose is not small, for the radium is only 1 or 2 mm. from the mucous membrane. Otolaryngologists might be inclined to feel that all they have to do is to buy or rent the proper radium applicator. The real difficulty is in judging whether or when such a damaging therapy is justified.

A therapeutic irradiation that has long been viewed askance by many radiologists is its use for epilation to cure ringworm of the scalp in children. In the early days when equipment was unreliable and measuring instruments unsatisfactory, alopecia was a frequent sequel. Today many radiologists and many dermatologists who do have adequate equipment nevertheless refuse to do therapeutic epilations. They feel that the chances that permanent alopecia will result are not negligible and that the blame for such an accident is beyond their willingness to face. This attitude seems less than worthy of our profession. If any patients with ringworm of the scalp need irradiation, then duty demands that one do it if technically equipped, or if not so equipped that one know whither to refer the patient to get it done.

Most cases of tinea capitis can be cleared quickly or slowly by local treatment with proper medicaments (iodine, fatty acids, etc). Some, especially Microsporon audouini, will not clear and would persist until puberty so alters the sebum as to make the soil no longer suitable for the organism. Epilation, however, results almost always in cure. Pulling the hairs by hand is so tedious as to be impractical. Roentgen epilation is practical and has been demonstrated to be safe, provided the technic is painstakingly correct. Even so, a perfectly even effect over the whole scalp seems almost impossible to attain. The dosage must be precise. Some careful radiologists measure the output of the tube immediately before every epilation treatment. When such care is taken alopecia rarely follows.

A conscientious radiologist might well equip himself to offer this service. He would undertake it in close consultation with the practitioner, with the help of a dermatologist if necessary. Considering recent advances in the topical (ointment) treatment of tinea capitis, he would insist that modern methods first be persistently and carefully applied under competent control for three months. He ought to have cultural proof that the infection is in fact M. audouini, that he is not dealing with mere reinfections from a mangy dog or cat. So safeguarded, one could conclude that a patient would be well advised to risk the tiny chance of alopecia in order to escape the overwhelming probability of persisting scalp infection throughout all the remaining years to puberty.

Roentgen treatment for benign conditions should be used only with a vivid appreciation of its capacity for harm and with an overt evaluation of its presumptive benefits weighed against the known and possible injuries inseparable from its use in effective dosage.

IN TIME OF PEACE

If current efforts at world organization for peace fail, military leaders warn that the next war will not be a declared war but might start with bombing or other attack on our large cities; overnight, they say, we may find ourselves with enormous refugee populations maimed, homeless and confused; industrial populations and rural populations may be attacked just as directly by means of new technics. Confusion will be "twice confounded" unless the medical and allied professions have somehow managed, through a process of preplanning and preexamination, to provide for the prior identification and physical fitness classification of every citizen for military or civilian duties in an all-out response of the entire population.

Accepting these warnings of military leaders at their face value, the medical and allied professions must organize still further to meet the nation's need. The following important services will be required in the months immediately ahead; first, developing a system for classifying all persons according to their physical fitness for military duty and for civilian duty; second, examination and classification of the population of cities of 100,000 and over; third, extension of these efforts

to the remainder of the population as rapidly as practicable, and, fourth, among other measures not directly medical in nature, assisting in developing a system for rapid personal identification.

The task will require the combined efforts of the medical and allied professions over months and perhaps years. The beginning of a rough but apparently usable system of classification is already available in the Physical Profile Serial used by the British and Canadian Armies in World War II and developed further and applied by our armed forces. The modification of this classification system to meet the needs of all civilian as well as military groups would not appear to be a too difficult task.

If the proper government authorities will make it plain as to what is actually needed, the medical profession will do its part. Though the leadership under current organization must come from other than the Defense Establishment, all efforts must be integrated with the military plans. Through the official bodies created by the House of Delegates and the Board of Trustees the American Medical Association can act promptly and efficiently.

Current Comment

INTERRELATIONS OF CANCER AND ARTERIOSCLEROSIS

Cancer and arteriosclerosis together account for about one half of all deaths. An examination of the general characteristics and of the factors contributing to the development of the two diseases yields evidence suggesting the possible existence of certain connections between them. Cancer as well as arteriosclerosis affects most often persons of middle or advanced age. Thus, a long preparatory or latent period seems to precede the manifestation of both conditions. Clinical and experimental evidence indicates that tissue anoxia may be involved in the production of cancer as well as of arteriosclerosis. Among the various causative agents known or suspected for both diseases cholesterol and its oxidation products assume a special place. For many years hypercholesterolemia and disturbances of the lipoid metabolism associated with diabetes mellitus and hypothyroidism have been related to the development of atherosclerosis. It is known, on the other hand, that endemic nontoxic nodular goiter is the main source of cancer of the thyroid,[1] while recent statistical analyses show that the incidence of cancer is higher in diabetic persons than the expected incidence among people of the general population.[2] It may not be, therefore, a mere coincidence that certain deficiency states involving the oxytropic and lipotropic factors of the vitamin B complex are related to disturbances of the lipoid metabolism favoring the development of atherosclerosis as well as of cirrhosis of the liver, with subsequent carcinoma of that organ.[3] The procarcinogenic action of biotin and fat and the anticarcinogenic effect of riboflavin on the production of hepatocarcinoma of rats given certain aromatic azo dyes furnish additional evidence in this respect. The occurrence of seasonal vitamin B deficiency has been related to the excessive incidence of precancerous and cancerous lesions of the oral and pharyngeal mucosa among the population of Northern Sweden, while the feeding of a diet deficient in choline and pyridoxine has caused in rats the appearance of papillomatous excrescences of the gastric mucosa and of primary cancer of the liver. Dietary ingestion of cholesterol has been used with contradictory results for stimulating in experimental animals the carcinogenic action of tar, crude paraffin oil and ultraviolet rays. Weil-Malherbe and Dickens[4] observed that the carcinogenic potency of 3,4-benzopyrene injected subcutaneously into mice was accentuated when this agent was dissolved in a 3 per cent solution of cholesterol in tricaprylin, while it was reduced when the chemical was administered in a tricaprylin solution containing 1.5 per cent lecithin. Cholesterol and lecithin seem to display in these experiments the same antagonism that they are known to possess in the development of atherosclerosis. Hieger[5] recently suggested that cholesterol itself might be a slow carcinogen or might be the carrier of small amounts of a potent carcinogen. Cholesterol seeds have been used for years as carriers of carcinogenic hydrocarbons in experimental work; it may be that this steroid exerts similar affinities and retaining properties for lipoid-soluble endogenous or exogenous carcinogens. Photochemical or thermic oxidation products of cholesterol have been related in recent years to the development of actinic cancer of the skin and of "dietary" cancer of the stomach.[6] Heuper observed in rats exposed to prolonged ultraviolet irradiation not only cancers of the skin, but also extensive arterial calcification. Similarly the development of leukemia and arteriocalcinosis has been observed[7] in mice fed a diet low in cystine and painted with an ethereal solution of methylcholanthrene. Finally, mention may be made of the not infrequent coexistence of endarteritic changes in the subcutaneous arteries and carcinomatous reactions of the epidermis in chronic radiodermatitis. Although the observations recorded do not permit definite conclusions as to the nature and existence of interrelations between cancer and arteriosclerosis, the evidence presented is sufficient to merit general attention.

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ORGANIZATION SECTION

JOINT COMMITTEE FOR THE COORDINATION OF MEDICAL ACTIVITIES

Abstract of Report of Meeting in Chicago, June 5

The meeting of the Joint Committee for the Coordination of Medical Activities was called to order by the Chairman, Dr. Ernest E. Irons, at 9:34 a. m., Saturday, June 5, 1948, in the Board Room of the American Medical Association Building in Chicago. Members and guests present were:

Dr. Donald G. Anderson, (A. M. A. Council on Medical Education and Hospitals)
Brig. Gen. George E. Armstrong (Office of the Surgeon General, U. S. Army)
Dr. Walter L. Bierring (Federation of State Medical Boards)
Mr. George W. Cooley (A. M. A. Council on Medical Service)
Mr. P. H. Costello (American Pharmaceutical Association)
Dr. W. Palmer Dearing (U. S. Public Health Service)
Dr. Warren F. Draper, (American Red Cross)
Capt. William E. Eaton (Office of the Surgeon General, U. S. Navy)
Dr. Lester J. Evans (American Medical Association)
Dr. Robert P. Fischelis (American Pharmaceutical Association)
Dr. Elmer L. Henderson (American Medical Association)
Dr. Ernest B. Howard (American Medical Association)
Dr. Ernest E. Irons (American College of Physicians)
Dr. George F. Lull (American Medical Association)
Capt. Frederick L. McDaniel (Bureau of Medicine and Surgery, U. S. Navy)
Dr. J. J. Moore (American Medical Association)
Dr. H. B. Mulholland (A. M. A. Committee on Rural Medical Service)
Dr. Howard C. Naffziger (American College of Surgeons)
Dr. Carl M. Peterson (A. M. A. Council on Industrial Health)
Col. Paul I. Robinson (Office of the Surgeon General, U. S. Army)
Dr. R. L. Sensenich (American Medical Association)
Dr. E. R. Serles (American Pharmaceutical Association)
Dr. H. H. Shoulders (American Medical Association)
Miss Mary E. Switzer (Federal Security Agency)

APPROVAL OF MINUTES OF MARCH 6 MEETING

The minutes of the meeting held on March 6, 1948, were approved after the Chairman had stated that minor corrections received by mail had been made.

NATIONAL HEALTH ASSEMBLY

Dr. Lull, a member of the Executive Committee of the National Health Assembly, reported as follows:

I am just one of a great number of physicians who attended the Assembly. A list of who was there, by organizations, is now being prepared and will be of interest; for instance, it will be found that the Red Cross had 40 representatives in attendance.

The Assembly went off far better than many of us expected it would. Most of my time and that of my associates was spent in the panel on medical care, which was quite heavily loaded with labor leaders of different types. The conduct of the men in this panel was such as to deserve favorable comment. All those who were representing organized medicine were willing to meet with other groups and discuss the problems; they had no fixed ideas. Since the meeting the labor groups have communicated with the Council on Medical Service and have expressed a desire to meet with representatives of the American Medical Association.

There were several interesting occurrences in the lobby: One was that a representative of a labor group said, "Why should we go out and fight for compulsory health insurance, for which we would have to pay taxes, when the trend is now for the employer to pay for it anyway?" However, that was not the attitude of the labor leaders in the meeting; they were "all out" for this type of health insurance.

The panel on chronic diseases was presided over by Dr. James R. Miller, an A. M. A. Trustee. Several other panels where there was adequate representation of the medical profession went along very quietly.

Mr. Ewing said he was not going to be bound by anything; that he was going to report to the President, and that he would draw up the ten year plan the President had requested regardless of what anyone else thought.

A notice was circulated from the *Mid-Month Survey* that the plan would be published this month. Dr. Fishbein contacted Mr. Ewing, who said that when it was released it would be released to all publications at the same time. The Executive Committee is to meet on June 28, after Mr. Ewing has reported to the President. Just what his report will be we do not yet know.

It was Miss Switzer's belief that of all the panels of the Assembly, the one on chronic diseases may have the most influence in devising a plan for the future. Dr. Mulholland thought that in the meetings of the Rural Health Section the farm groups and the doctors got much closer together in trying to solve some of their problems, realizing that each group had something to offer the other. Drs. Bierring and Mulholland spoke of discussions in the Rural Health Section wherein the farm groups were vociferous in demanding that there be more medical schools, and Dr. Dearing said that the whole group of rural people are worked up about their inability to get as much service as they think they need. It was Dr. Bierring's opinion that the discussions in the Section on Environmental Sanitation were very constructive.

NATIONAL CONFERENCE ON FAMILY LIFE

Miss Switzer presented the following report:

The National Conference on Family Life took place at the end of the week in which the National Health Assembly was held, and it was not possible for me to attend very many of the sessions. No recommendations, as such, came out of the Conference except a plea to work together to improve family life in general. On the whole, the background material sent ahead of time to the participants seemed to please them. Most of the time of the section on medical care was spent in editing the advance material, which, generally, seems to have been found useful by the educational groups. Most of the publicity given the Conference was concerned with the discussions in the section on sterility. The Conference was an experiment. If its proceedings are circulated widely, attention will be focused on certain problems that will give community groups something for which to work. It was well worth while, and nothing radical or revolutionary came out of it; it was a constructive move.

BIPARTISAN COMMITTEE ON REORGANIZATION OF FEDERAL AGENCIES

Dr. Dearing said: The Public Health Service is a sort of "guinea pig" in this connection. Various studies are being farmed out to nongovernment concerns. An outside group is studying the government service as a career, picking out persons in individual jobs and interviewing them. There are two groups within the Bipartisan Committee that are concerning themselves with the branches of the government having to do with medical affairs; one is that of which Mr. Tracy Voorhees is chairman and the other is the Brookings Institution, which is now responsible for studying public health activities. These two groups are working together to some extent. Then there is a task force on field organization; that is, on the relation of the Government to the states. The organization of the Bipartisan Committee is about as complicated as that of the Government itself.

RURAL MEDICAL SERVICE

Dr. Mulholland presented the following report on the activities of the American Medical Association's Committee on Rural Medical Service:

The employment of a field representative for the Committee on Rural Medical Service was recently authorized, and we are now negotiating with a highly qualified person who can be sent out to explore what is being done in the various states. We think this activity will cause the farm people to feel that we really are trying to do something down to the "grass roots" level.

On June 25 the executive committee of the Council on Medical Service and the executive committee of the Committee on Rural Medical Service are to meet with the cooperative health group here in Chicago. This will be the first of a series of exploratory conferences to find a common ground with the health cooperatives. Similar conferences will be held with labor organiations. We propose to have a meeting in the fall with representatives of farm groups and organizations to bring together with those farm groups all of the state chairmen of the Committee on Rural Medical Service. We feel that our February Congress on Rural Health does not draw in enough doctors on the state level.

Our Committee will have an exhibit at the Chicago Session of the American Medical Association this month, which will be a practical demonstration of what has been and is being done in several states to try to solve the problems of medical service in the rural areas.

Dr. Shoulders asked Dr. Mulholland whether he had observed any trend since the war for physicians to go to small towns and rural areas to practice, which was not the case previously; the reply was that there is such a trend and that the secretary of the Committee on Rural Medical Service, had stated that there is no difficulty in getting a doctor to go into a community of 1,000 persons where there are good facilities for practice.

In reply to a question by the Chairman whether or not the people in all these small communities actually need a physician, Dr. Mulholland said, "They think they do," and also stated that the Committee on Rural Medical Service is attempting to make an up-to-date compilation of actually needy areas.

Chairman Irons spoke as follows:

I am much impressed with the trend of discussions in this country as illustrated by the reports on the National Health Assembly, the National Conference on Family Life, the Bipartisan Committee, and so on. All of this, it seems to me, is a voluntary attempt on the part of those who have done some thinking on the subject to improve the technic of living together. It has to do with the social motivations which underlie practically everything we do. Divergence of opinion lies not in the desirability of our relations with each other or our methods of doing things but in the methods of cure of the faults we discover. That has been true throughout history. The faults of social living together, the results of invention drawing people together in larger and larger communities and the fact that rising standards of living introduce continually new problems and new things for people to want all are combined in what might be called social motivations, which underlie not only medicine but all social relations. The difficulty is not that we do not recognize the necessity of alleviating social injustice but that we do not agree on the method of cure. What we physicians have in mind is to prevent, if possible, the introduction of methods of cure that have always failed throughout all history. The fact that we freely and openly discuss all these diverse questions here is an encouraging feature of the national thinking.

HOSPITAL SURVEY AND CONSTRUCTION PROGRAM

Dr. Dearing reported as follows:

At present the Hospital Survey and Construction Act provides that if a state has not enacted provisions for establishing and enforcing minimum standards of maintenance and operation by July 1, 1948, such state will become ineligible for all time for further participation in the program. A Bill now pending, HR-6339, provides that passage of provisions for enforcement of minimum standards of maintenance and operation, after the July 1, 1948, deadline, will reinstate such state to eligibility for a federal allotment in the Hospital Survey and Construction Program. This bill passed the House on May 18 and was referred to the Senate Committee on Labor and Public Welfare. There has been no further action on it. Only one state is not under the wire.

Four states, Delaware, Nevada, Rhode Island and Wyoming, have not yet submitted state plans.

The number of projects approved and the cost involved are:

	No.	Total Cost	Federal Share
Initial applications approved	285	$131,385,812	$37,935,201
Complete applications approved	34	13,610,851	4,039,268
Totals	319	$144,996,663	$41,974,469

Distribution of projects by type of facility:

General hospitals	226
Mental hospitals	22
Tuberculosis hospitals	16
Chronic disease hospitals	4
Health centers	45
Other (nurses' home, lab., etc.)	6
Total	319

Analysis of approved general hospital projects:

Forty-three per cent of the total number of applications approved represent projects in towns having a population under 2,500. Eighty-two per cent of the total applications approved are for projects in towns under 10,000 population. Ten per cent of the applications approved represent projects of 100 beds or over. The average is approximately 50 beds. Seventy-five per cent of the hospital projects are located in areas designated as "rural" by state agencies. Sixty-three per cent of the approved projects are located in "A" priority areas.

Payments of federal funds:

Roanoke-Chowan General Hospital, Ahoskie, N. C.	$ 12,806.30
Suwannee County General Hospital, Live Oak, Fla.	28,275.90
Duval County Hospital, Jacksonville, Fla.	70,828.01
Jefferson County Health Center, Birmingham, Ala.	156,681.03
Number of Payments—4, totaling	$268,591.24

A UNIFORM PHARMACY PRACTICE ACT

The following progress report was presented by Dr. Serles:

I would first call your attention to a decision in what is referred to as the Sullivan Case, which clearly places the responsibility of the physician and the pharmacist in saying that a label on a pharmaceutical product must definitely state that the product can be sold only on prescription. The physician should bear well in mind that he should not suggest to patients that they may purchase a familiarly named item which clearly calls for a prescription. In attempting to protect the patient, medication is the responsibility of the physician and of the pharmacist who conforms in meeting requirements by not offering for sale any items not covered.

Extensive study is being given to the development of a Uniform Pharmacy Practice Act, and a committee will soon present a draft of a statute which can be formally considered by this group.

I should like to enlist the thinking of this Joint Committee on a situation which seems to be developing throughout the country, part of which seems to be a desire to make drugs more readily available to patients. I refer to the practice of writing full directions on pharmacal products. In following such a program, the thought is that it gives a fine advantage to the patient, helping him to procure what he needs. The American Pharmaceutical Association would take the very definite stand that preparations which contain potent drugs certainly could not have a single direction printed for all conditions. That is to say, we all know there is not one set of directions for all uses of a product offered on the market.

The discussion of Dr. Serles' statement was as follows:

Dr. Fischelis: There appears to be a disposition on the part of the patent medicine industry to take advantage of the position of the Food and Drug Administration in this matter, which is that the Administration leans over backward in trying to show that it is not using the Food, Drug and Cosmetic Act to discourage self medication but is trying to make self medication safe and, to that extent, is insisting that labels contain certain warnings. That, however, presumes some knowledge of medicine on the part of the patient; of course, the patent medicine industry says: "What the Food and Drug Administration has endorsed is the only thing we are putting on the market."

Miss Switzer: I believe that the integrity of the Food and Drug Administration has been sufficiently established that it might be possible for it to take a little different attitude, and perhaps it ought to revamp its point of view on this. It might be desirable to give some thought in the discussion of the Uniform Pharmacy Practice Act to how the Administration might be brought in and asked to review the situation. The thinking of the Administration is changing in many ways; they recognize that the pioneer days are past and that the primary problem is not policing.

Captain Eaton: Is anything being done or can anything be done to control the tremendous advertising of aspirin, particularly over the radio?

Doctor Serles: The only control would be a crystallized public opinion. Another enormous class of products needing additional control includes the insecticides, fungicides, etc., that are brought into household use. In every store of a certain chain grocery concern you will find a 10 foot counter with a display of every possible pharmacal item it can contain.

Dr. Fischelis: There is another point on which the stand of the pharmaceutical profession has been misunderstood, and that is the matter of channeling all sales of drugs through the pharmacies. The argument against it is that anybody who can make a label or make change ought to be able to sell drug products, but there is a great difference in having these drugs handled by men who have had education in the administration and use of drugs and men who are only merchandizers. The state under its police power regulates the practice of a pharmacy, but there is no such power with respect to a grocery store.

It was moved, seconded and carried, that the Food and Drug Administration be invited to send a representative to the meetings of the Joint Committee.

AMERICAN RED CROSS BLOOD BANK PROGRAM

Dr. Draper presented the following statement:

The National Blood Program has been progressing very successfully and very smoothly. In addition to the six centers mentioned at the last meeting of this committee three new centers have been opened, one at Tucson, Ariz., one at San Jose and one at Los Angeles, Calif. The program is now serving the blood requirements of six or seven million people, which is not a bad record for the first year. There has been no difficulty whatever in getting all of the blood required in the areas served. There has been no complaint or any criticism at all from any of the national blood centers. The physicians and the hospitals have all expressed themselves as being much pleased. For the first time it has been possible to undertake operations requiring a great deal of blood which the surgeons would not have undertaken if the supply had not been satisfactory.

As you know, prior to the National Blood Program, there was a local program of the Red Cross known as a Permissive Program, which was simply an arrangement whereby the local Red Cross chapter entered into an agreement with the local medical society under which the chapter agreed to recruit donors. Roughly, some 35 communities are operating on this Permissive Program. It is not ideal but has to be kept on until the national program can catch up and absorb it. Criticisms that do occur come from these diverse local programs, and now and then some Red Cross chapter does some unfortunate thing which ought not to have been done. The Red Cross can not apply the iron fist to prevent difficulties from sometimes happening.

The Red Cross approached this matter in the very finest way it could and received the approval, in principle, of the American Medical Association and the approval of other national agencies. It is inconceivable that the program could be defeated now. Furthermore a situation of national emergency may be developing. The Red Cross certainly is not going to give up its program; it would have to go before the public.

The committee which was authorized by the House of Delegates of the American Medical Association to study the Red Cross Blood Bank Program has formulated its report, which was published in THE JOURNAL for May 8, 1948. The Red Cross has accepted everything that the House of Delegates has asked it to accept and has played ball straight down the middle of the fairway.

WORLD MEDICAL ASSOCIATION

The following information was presented by Dr. Irons:

The office of the World Medical Association has been established in the building of the New York Academy of Medicine. A meeting of the Council was held in New York during the last week in April. This meeting was very harmonious, quite different from the one in Paris in 1947 when a rather serious time was had with a communistic element which tried to disrupt the organization. The meeting in New York lasted for three days. An Executive Secretary was elected in the person of Dr. Louis H. Bauer of Hempstead, N. Y., who is a member of the Board of Trustees of the American Medical Association and a past president of the Medical Society of the State of New York and is prominent in many other ways in medical affairs in this country. Dr. Bauer has been persuaded to take over his work temporarily and perhaps, if necessary, will later give it his full time.

A meeting of the full Assembly of the World Medical Association had been planned for September in Prague, but after what happened in Czechoslovakia a while ago it was felt that it would not be wise to meet there. It appeared that representatives of two nations would not be welcome in Czechoslovakia, so the meeting was changed to Geneva, Switzerland, and will take place on September 5, 6 and 7, 1948.

The Council meeting in New York was quite interesting. The member from Czechoslovakia not only brought invitations for the officers and

Council to bring the Assembly to that country but also announced that the government would entertain the Council at some resort for two weeks with all expenses paid. Following the New York meeting, the Council was entertained by a number of universities, visited American Medical Association headquarters in Chicago and spent about a week in Rochester, Minn. The members from foreign countries were presented with Honorary Fellowships in Alpha Omega Alpha while they were in Chicago. The World Medical Association seems to be well on its way.

To back up the World Medical Association the United States Committee has been formed, the funds for which are coming from contributions from the larger medical organizations, the pharmaceutical industry and individuals. Contributions of $10,000 have been received from several, and there are also $10.00 contributions from Founder Members. The United States Committee has undertaken to finance the World Medical Association for five years. It is a big undertaking, but it is felt that it can be done with the support of the medical profession and the pharmaceutical industry.

Dr. Henderson said that each nation has two delegates in the General Assembly and that he and Dr. Sensenich will represent the American Medical Association as delegates to the meeting in Geneva. He added that forty-nine different nations were represented at the meeting in Paris last year.

WORLD HEALTH ORGANIZATION

Miss Switzer commented on the World Health Organization (U.N.) which is to have an assembly in Geneva this month—June 1948—saying that it now appears that the United States will send a delegation. The constitution of the World Health Organization stipulates that preferably the head of the delegation shall be the chief health officer of the government, and it now seems certain that Dr. Thomas Parran will fill that place.

CAREER GUIDANCE AND CLASSIFICATION OF ARMY MEDICAL OFFICERS

Following is an abstract of a statement presented by Colonel Robinson:

For the past three or four years the Surgeon General of the Army has been working on improving methods of personnel management in the medical department. The work thus far accomplished can be divided into three general headings: (1) classification methods; (2) career patterns; (3) management control system.

I want to emphasize that career patterns are in existence for every specialty now utilized in the practice of medicine in the Army.

The Army is now fully prepared to determine its requirements by specialty and by qualifications within the specialty for all medical officers. It is expected that within a relatively short time we shall be able to do this for all Corps within the medical department. Both our procurement program and our training program are now geared to the Career Management System. It is being projected into our Reserve Corps. In order that this knowledge may be utilized to prevent wastage of personnel in future emergencies, it is thought that a like classification scheme should be more universally adopted within the profession. This classification system can be readily adapted to the profession as a whole or any designated part of it (for example, any age group). It is thought that this system is the greatest single contribution to efficient utilization of medical personnel, both in peace and in war, that has yet been conceived.

Dr. Dearing stated that the Public Health Service concurs absolutely with Colonel Robinson's final statement and thinks this is the finest job of working out a plan and system that ever has been done; it is completely applicable to the work of the Service, which is taking steps to adopt it as rapidly as possible with some small differences in the major breakdown. He added: The timeliness of this plan in connection with the work that the National Security Resources Board is undertaking is interesting; professional organizations are being asked to consider the problem of compiling and keeping up a roster of physicians in the country according to a uniform classification system which would be agreed to by the profession and the Government, and certainly this plan is made to order for implementing that program.

Miss Switzer asked how soon it could be determined which line of medical practice an officer will undertake and at what point the potentialities are reviewed and decision made that he shall become a specialist. Colonel Robinson's answer was: At present the individual desires of the officer and the fact that he makes good himself prevail; however, our next project is to contrive some plan whereby we can determine by a scientific method the individual's adaptability; it is intended always in this system that the individual's desire shall be the predominant factor.

At a recent meeting in Washington where a Civil Defense plan was discussed it was proposed that the same kind of rating system described by Colonel Robinson might be applied to the whole medical profession so that the record of each physician would bear his rating number. Dr. Sensenich doubted the practicability of any agency's putting itself in a position to attach a number to a physician in civil life regardless of whether the system might seem useful. The Chairman agreed with Dr. Sensenich.

STATEMENTS FROM LIAISON MEMBERS

Dr. Evans in referring to the discussion on the National Health Assembly stated: I sat through three days of the Rural Health Panel, and I have never heard such fine talks. The progress made over the years has been phenomenal, and most gratifying are the attitudes exhibited, as well as the fact that people seem to think that it will open up and make more free the relationships between the people who are concerned with health.

Dr. Bierring informed the Committee that another specialty board is on the way, to be called the American Board of Preventive Medicine and Public Health Physicians. It is to consist of nine members, three from the American Public Health Association, three from the Section on Preventive and Industrial Medicine and Public Health of the American Medical Association, one from the Southern Medical Association, one from the Canadian Public Health Association, and one from the group of university schools of public health. First steps were taken in February. It is to meet the need of the physicians engaged now and in the future in a full time career in preventive medicine and public health.

Dr. Bierring stated: A matter that still is of considerable concern to licensing bodies is the problem of recognition and licensure of graduates of the two unrecognized medical schools in this country. One, of course, is now out of existence, but its graduates are applying for license in other states. Many of them have completed internships and residencies and some have had military service; perhaps these may be eligible for license. The question is whether these graduates by subsequent study and experience may have acquired sufficient ability to warrant licensing them.

Captain Eaton presented for the Committee's official records a transcript of discussions in a symposium conducted in the Office of the Surgeon General of the Navy in May to which all senior medical officers were called.

Captain McDaniel gave the following report:

The Navy Department has 180 interns, graduates of medical schools since February 1948, who have accepted appointment for Naval internship for the years 1948 and 1949 in Naval hospitals. During the years 1947 and 1948, the Navy had 71 interns in its hospitals.

In addition to this number of interns for Naval hospitals, arrangements are being firmed up whereby approximately 100 interns will be placed in civilian institutions. These interns will be members of the Naval Reserve by voluntary enrolment. They will be reserve officers in fact and will receive all pay and allowances of a lieutenant (junior grade) of the Navy, including the $100 per month additional pay now allowed medical officers in accordance with Public Law 365, 80th Congress.

It should be pointed out that these additional 100 interns will serve in civilian institutions and therefore will not be an additional drain from the civilian institutions.

REPRESENTATION FROM VETERANS ADMINISTRATION AND AMERICAN DENTAL ASSOCIATION

The Chairman brought to the attention of the Committee the fact that no representative from the Veterans Administration or the American Dental Association had been present at Committee meetings for some time. The Committee requested the Chairman to communicate with the Dental Association and the Veterans Administration, emphasizing the desire of the members that there be a renewal of attendance.

REPORT TO HOUSE OF DELEGATES OF AMERICAN MEDICAL ASSOCIATION

It was moved by Dr. Henderson, seconded by Dr. Sensenich, and carried, that the Chairman prepare a report of the past year's activity for presentation to the House of Delegates of the American Medical Association at its meeting in Chicago on June 21 to 25.

NEXT MEETING

The Joint Committee decided to hold its next meeting at American Medical Association headquarters in Chicago at 9:30 a. m., Saturday, Sept. 25, 1948.

The meeting adjourned at 12:50 p. m.

GOVERNMENT SERVICES

ARMY

INSTITUTE FOR PSYCHOTHERAPEUTIC MEDICINE

As part of the Medical Department's program of close cooperation and consultation with civilian doctors, courses in psychotherapeutic medicine were held simultaneously for two weeks beginning September 6 at the Walter Reed General Hospital, Washington, D. C., Letterman General Hospital, San Francisco, and Fitzsimons General Hospital, Denver. Among the ten specialists participating in the course given at the Walter Reed General Hospital were Drs. Thomas A. Loftus, New York; Charlotte Babcock, Chicago; Meyer A. Zeligs, San Francisco; Jacques S. Gottlieb, Iowa City, and Bernard C. Glueck Jr., Ossining, N. Y.

BENEFITS FOR ARMY NURSES

Nurses newly commissioned in the Army Nurse Corps Reserve who have not had prior military experience and who request and accept extended active duty will be given an allowance of $250 to cover the cost of initial purchase of uniforms. Extended active duty means that the reserve nurse agrees to serve in an Army hospital for not less than one year. Reserve nurses enrolled in the extension courses now available through the Medical Field Service School will earn credit hours for the courses completed, and these hours will count toward eligibility for promotion and retirement. This applies to all reserve nurses regardless of whether or not they have requested and/or accepted extended active duty. Six complete extension course series are now available for Army Nurse Corps Reserve officers up through the grade of major. Information may be obtained from the Department of Extension Courses, Medical Field Service School, Fort Sam Houston, Texas.

CIVILIAN SPECIALISTS ELIGIBLE FOR RESERVE COMMISSIONS

The Department of the Army announces that civilian specialists in any of seventy-six broadly defined professional and technical specialties may be tendered commissions ranging from second lieutenant to colonel if they apply and qualify. The applicants must be at least 21 years of age and not more than 55. No previous military experience is required. All must be citizens of the United States. In the list of specialties essential to the needs of the Army are, among others, medicine, nursing, nutrition, pharmacy, biochemistry, bacteriology, parasitology, optometry, serology, toxicology and industrial hygiene.

LIBRARIANS WANTED

The Army Medical Library is in need of librarians with medical training or experience, also cataloging experience and foreign language qualifications. For details, write to the Personnel Officer, Army Medical Library, 7th and Independence Avenue, S. W., Washington 25, D. C.

PUBLIC HEALTH SERVICE

NATIONAL ADVISORY HEART COUNCIL

In accordance with the National Heart Act of June 16, 1948, the Surgeon General has appointed the following twelve members of the National Advisory Heart Council:

Dr. Paul D. White, Boston, who will serve as executive chairman of the council.

Dr. C. A. Elvehjem, Madison, Wis., dean of graduate schools, University of Wisconsin.

Dr. Tinsley Harrison, Dallas, Texas, professor of internal medicine, Southwestern Medical College.

Dr. Irvine H. Page, Cleveland, Ohio, director of research, Cleveland Clinic Foundation.

Dr. Burrell O. Raulston, Los Angeles, dean, University of Southern California Medical School.

Dr. T. Duckett Jones, New York, medical director, Helen Hay Whitney Foundation.

Mr. James S. Adams, New York, director, American Cancer Society.

Mr. Maurice Goldblatt, Chicago, president, University of Chicago Cancer Research Foundation.

Mrs. Albert D. Lasker, New York, co-founder, Albert and Mary Lasker Foundation for education and medical research.

Mr. E. B. MacNaughton, Portland, trustee, Good Samaritan Hospital, Portland.

Mr. Ernst Mahler, Neenah, Wis., executive vice president, Kimberly-Clark Corporation.

Mr. Albert J. Wolf, New Orleans, president, board of trustees, Touro Infirmary, New Orleans.

The law requires that six of the members of the council be outstanding experts in the study, diagnosis and treatment of heart diseases. The duties of the council are to advise with the National Heart Institute in developing research programs to help in the attack on cardiovascular diseases; to make recommendations to the Surgeon General on applications of institutions or individuals for research and training grants; to make a worldwide collection of information on research in heart diseases, and to advise on the entire program of the National Heart Institute for controlling cardiovascular diseases. The first meeting of the council was held September 8 at the National Institute of Health, Bethesda, Md.

NATIONAL HOSPITAL FOR TREATMENT OF HANSEN'S DISEASE

The picture is that of the United States Marine Hospital at Carville, La., which is the only institution in the United States devoted exclusively to the care of patients with Hansen's disease (leprosy). This hospital was formerly a Louisiana state hospital but was taken over by the federal government in 1921 and its facilities made available to any citizen of the United States. All building have been replaced by modern fire-resistant structures, and the hospital has a class A rating. There are no charges to patients, and it is the object of the

U. S. Marine Hospital, Carville, La.

Public Health Service which administers this hospital to encourage the greatest liberty to the patient compatible with the accomplishment of the purposes of the hospital. There is a broad field of activities including sports and other recreations for patients, and a monthly publication, *The Star,* published by the patients. The average daily census according to our latest figures was 379. Active treatment is carried on with the newer drugs. During 1946, 43 patients were discharged from this hospital.

PHYSICIANS SEPARATED FROM SERVICE

ARMY MEDICAL CORPS OFFICERS RECOMMENDED FOR/OR RELIEVED FROM ACTIVE DUTY

Alabama

Cloyd, Walter L.....Tarrant
Fowlkes, Thomas C.....Selma
Gewin, Henry M.....Mobile
Harris, Robert O. III.....Mobile
Mills, Clarence W. Jr.....Fairfield

Arizona

Jameson, Sam G.....Mangolia
Millett, Douglas K.....Mesa
Stapley, Lorel A. Jr.....Phoenix

California

Bayless, Allan E.....Los Angeles
Bonar, Samuel C.....Upland
Ellis, John F.....San Francisco
Lambert, Richard G.....San Francisco
Loring, Theodore W.....Palo Alto
Medefind, John N.....Fresno
Moore, William H. Jr.....Bakersfield
Mortensen, J. D.....Los Angeles
Schaffner, Marlowe H.....Los Angeles
Scott, Wirt S. Jr.....San Francisco
Stewart, James J.....San Marino
Williams, Robert E.....Glendale

Colorado

Stewart, Robert J.....Denver

District of Columbia

Harris, Lester F.....Washington
St. John, Joseph H.....Washington

Florida

Lindau, Warren.....Miami Beach
McCallister, Archie.....Tallahassee

Georgia

Bell, Ira E. Jr.....Middleton
Black, Grady E.....Valdosta
Brackett, John G.....East Point
Hicks, Wright G.....Roberta
Luke, Chester K.....Atlanta
Thoroughman, James C.....Atlanta
Van Sant, Thomas J. Jr.....Woodstock

Idaho

Murphy, Jack Tullus.....Rupert
Smith, Dale H.....Idaho Falls

Illinois

Altman, George L.....Chicago
Atkins, Robert A.....Sumner
Bernstein, Lionel M.....Chicago
Case, John B.....Chicago
Edwards, Howard M. Jr.....Dixon
Elliott, Thomas A.....Chicago
Giammasi, Louis N.....Chicago
Gordon, Archer S.....Aurora
Hobson, Edwin R.....Gillespie
Kendall, Edward A. Jr.....Granite City
Long, John S.....Pontiac
Milos, Robert J.....Chicago
Munson, Thomas Arndt.....Metcalf
Muraskas, Edward B.....Chicago
Murphy, Joseph W.....Park Ridge
Petrone, Gerald J.....Chicago
Phares, Walter S.....Chicago
Pilz, Clifford G.....Chicago
Quilty, Thomas J.....Moline
Richmond, Thomas E.....St. Charles
Simon, Arnold B.....Chicago
Springer, Donald W.....Oak Park
Strueh, Paul E.....Chicago
Wilson, William C.....Glen Ellyn
Wolfe, Gordon F.....Elgin
Young, William H. Jr.....Elgin

Indiana

Carter, Fred S.....Hammond
Harger, Robert W.....Indianapolis
Klotz, Joseph G.....Noblesville

Indiana—Continued

Mendez, Fernando L. Jr.....South Bend
Saint, William K.....Newcastle
Squire, Robert M.....Lyons
Van Kirk, Paul P.....Frankfort

Iowa

Goodwin, Laurence D.....Iowa City
Green, Robert P.....Marshalltown
Kardon, Harold E.....Des Moines
Kaskie, Clifford R.....Des Moines
Penly, Richard S.....South Newton
Skelley, Paul B.....Clinton
Weston, Robert A. Jr.....Des Moines

Kansas

Batty, James J.....Kansas City
Dlabal, Frank A.....Wilson
Kidder, Lewis A.....Pittsburg
McAuley, Arthur A.....Kansas City
Nelson, Theodore A.....Phillipsburg

Kentucky

Cahoon, Reynolds F.....Louisville
Cloyd, William H.....Lexington
Combs, Gene N.....Langley
Doyle, George F.....Winchester
Haynes, Allan L.....Louisville
Jarvis, Richard B.....Louisville
Ploetner, Edward J.....Louisville
Stubblefield, Robert J.....Murray

Maine

Lockhart, Philip B.....Pemaquid

Maryland

Canter, Nathan.....Baltimore
Jones, Philip E.....Rock Hall
Klinefelter, Harry F. Jr.....Baltimore
Rudo, Marvin.....Baltimore
Stedem, Anthony F.....Baltimore
Thompson, LeRoy K.....Hyattsville

Massachusetts

Bradford, Martin L.....Sharon
Carey, Edward G.....Boston
Lamothe, Paul A.....Arlington
Levin, Melvin H.....Winthrop
Lowry, Paul Thorpe.....Cambridge
McGowan, John A. Jr.....Medford
MacPherson, Donald H.....Quincy
Meilman, Edward.....Roxbury
Metcalf, William.....Roxbury
Paushter, Matthew H.....Springfield
Sweeney, Guy R.....Medford

Michigan

Fielder, Charles R.....Grosse Pointe
Frayer, William C.....Ann Arbor
Ketchum, Hall.....Muskegon Hgts.
Maltzer, Joseph H.....Detroit
Mazur, Theodore T.....Detroit
Mount, Frank W.....Royal Oak
Posthuma, Albert E.....Grand Rapids
Richey, Bert R.....Detroit
Talso, Peter J.....Ishpeming
Turner, John J. Jr.....Highland Park
Woodward, Sheldon C.....Flint

Minnesota

Ballinger, Carter M.....Stillwater
Breneman, James C.....Sherburn
DuBois, Julian F. Jr.....Sauk Centre
Karon, Allan B.....St. Paul
Kucera, William J.....Minneapolis
Mazzitello, William F.....St. Paul
Mundahl, Harold R.....Fairfax
Nelimark, Donald R.....Virginia
Parks, Raymond E.....St. Paul
Petersen, William Earl.....St. Paul
Rynda, Edwin R.....New Prague

Missouri

Conrad, Marshall B.....Webster Groves
Dietrich, Alfred G.....Kansas City
Petzold, Howard V.....Joplin

Montana

Murphy, James E.....Whitefish

Nebraska

Davies, Louis T.....Omaha

New Jersey

Bornstein, Leo A.....Jersey City
Carmona, Manuel G.....Tuckerton
Dalrymple, Robert M.....Morristown
Durham, Frederick W.....Camden
Garrett, Thomas A.....Jersey City
Kerr, Andrew D. Jr.....Clifton
Longley, Stephen B.....Madison
O'Connor, Thomas W.....Westfield
Rothfeld, Benjamin.....Newark
Santo, Ralph Verrei.....Newark
Selvage, Irving L. Jr.....South Orange
Sklansky, Morris A.....Bloomfield
Vanderbush, Edward F.....Hewitt

New Mexico

Shy, George M.....Albuquerque

New York

Ackermann, Kurt.....New York
Argentieri, Mario A.....Hornell
Barron, Leonard J.....New York
Berg, Seymour.....Bronx
Bloom, Samuel M.....Brooklyn
Cohen, Herbert.....Brooklyn
Cotler, Samuel.....Bronx
Downey, Martin J. Jr.....Buffalo
Gersh, Marvin J.....New York
Gregware, Peter R.....Troy
Herschfus, Jechiel A.....New York
Heslin, Thomas M.....Brooklyn
Hunter, Harry D.....Rochester
Hurwitz, Mervin H.....Richmond Hill
Jameson, John W.....Rochester
Katz, Burton.....Brooklyn
Mahr, Merle M.....New York
Molyneaux, Eva W.....Buffalo
Powers, Samuel R. Jr.....New York
Schortman, Edward F.....New York
Tybring, Gilbert B. Jr.....Endicott
Walsh, Robert J.....New York
Winkelman, Herman.....Scotia

North Carolina

Flower, Arthur H. Jr.....Durham
Harrelson, Rose C. Jr.....Tabor City
McLean, Augustus A. Jr.....Lenoir
McMurry, Avery W.....Shelby
Moore, Edward E.....Biltmore
Murray, E. Cotter.....Roanoke Rapids
Nicholson, Francis.....Durham

Tennessee

Boone, Howard A.....Memphis
Noel, Oscar F.....Nashville
Qualls, Donald M.....Livingston

Utah

Dovey, Edward G.....Salt Lake City
Kartchner, Fred D.....W. Provo

Vermont

Higgins, James F.....Barre

Virginia

Bell, Lewis F.....Valley Pike
Kelly, Frank R. Jr.....Richmond
Miller, Lawrence S.....Bridgewater
St. Clair, Harvey R.....Staunton

England

Miller, Leroy D.....London

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

COLORADO

Postgraduate Courses.—A postgraduate course in public health and preventive medicine, to be sponsored by the Colorado State Medical Society, the University of Colorado School of Medicine, the Colorado State Department of Public Health and the U. S. Public Health Service, will be given at the University of Colorado Medical Center, Denver, October 18-21. The course has been designed to cover in practical fashion the fundamentals of communicable disease control. Although designed primarily for general practitioners in rural areas, the course is open to all physicians.——A short course for physicians on problems of newborn infants will be given October 14-16 by the University of Colorado School of Medicine and the Colorado State Department of Health, Denver. Lectures, panel discussions and demonstrations will be given by members of the faculty on obstetric aspects of prematurity, resuscitation, isoimmunization, psychologic problems developing in prematurely born infants, community planning, interpretation of laboratory findings in the newborn and parenteral fluid therapy. A registration fee of $10 is required. Inquiries should be directed to Dr. Frode Jensen, Director of Graduate and Postgraduate Education, University of Colorado Medical Center, Denver.

FLORIDA

Typhus Control in Florida.—The state board of health reports that in those Florida counties carrying out organized typhus measures for 1947 a 46 per cent reduction in reported typhus cases was evident over the previous year. In comparison, there was a 64 per cent increase in the combined number of reported cases from those counties where no organized control work was performed. The number of cases of endemic typhus has increased since it first was officially reported in 1918 to a peak of 484 cases in 1944. The state board of health is concentrating its control program in counties where the greatest number of cases have been reported. Rat-proofing of buildings, distribution of poisoned rat bait, rat trapping, promoting better garbage disposal methods and distribution of DDT dust in and around buildings are being used.

GEORGIA

Greensboro Hospital.—Construction of the Minnie G. Boswell Memorial Hospital, the first hospital to be erected in the state under the provisions of the Hill-Burton Act, was recently begun in Greensboro; it is expected to be completed in ten months.

Postgraduate Course in Medicine and Surgery.—Emory University School of Medicine, Atlanta, in cooperation with the Medical Association of Georgia will present a postgraduate course in medicine and surgery October 11-15. The course is designed to present current ideas concerning the diagnostic and therapeutic problems of general practice and may be used in meeting part of the requirements for membership in the American Academy of General Practice. The registration fee is $10.

ILLINOIS

Incidence of Infectious Diseases.—Venereal diseases are by far the most widely prevalent communicable infections in Illinois. As of August 14, according to the state health department, 10,564 cases of syphilis had been reported. The morbidity report for the first thirty-two weeks of this year shows a 17 per cent reduction in the incidence of tuberculosis. A total of 4,061 cases have been reported so far this year, as against 4,918 in the 1947 period. Marked reductions have also been noted in the acute diseases of the respiratory tract. Only 90 cases of influenza had been reported, as compared with 1,068 in the same period last year. Whooping cough, with 1,517 cases, was a little more than half as prevalent as last year. Diphtheria declined to 74 cases, and typhoid to 59 cases. There were 41,570 cases of measles reported, as compared with 4,018 cases last year. Mumps, with 9,970 cases, is more than twice as prevalent as last year, and poliomyelitis has been responsible for 230 reported cases of illness as against 124 in the 1947 period.

Chicago

Virus and Rickettsial Diagnostic Tests.—The department of bacteriology at Micheal Reese Hospital has introduced routine virus and rickettsial diagnostic tests. This hospital is said to be one of the first in this area to offer these tests on a routine basis.

Illinois Faculty Promotions.—Eight members of the faculty of the University of Illinois College of Medicine have recently received professorial promotions. Dr. Cecil A. Krakower has been promoted to the rank of professor of pathology and will also serve as associate pathologist in the university's 428 bed research and educational hospitals. Dr. Fay H. Squire has been made clinical professor of radiology. The rank of associate professor has been given to Dr. Morton I. Grossman, physiology, and Dr. Georgiana D. Theobald, ophthalmology. Assistant professorships have been awarded to the following: Dr. Matthew J. Brunner, dermatology; Hubert R. Catchpole, Ph.D., physiology; Miss Ruth B. Coleman, A.B., medical illustration, and Dr. Joseph S. Haas, ophthalmology.

INDIANA

Dr. Ross to Head Department.—Dr. Alexander T. Ross, assistant professor of neurology and psychiatry in the Indiana University School of Medicine, Bloomington-Indianapolis, has been named to succeed Dr. David A. Boyd Jr., who has resigned as chairman of the department of neurology and psychiatry. Dr. Ross will become a full time member of the staff with the rank of professor of neurology. Appointment of a professor of psychiatry will be made later. Dr. Boyd, professor of psychiatry and chairman of the department for nearly ten years, resigned to become consultant in psychiatry at the Mayo Clinic, Rochester, Minn., in the development of its psychiatric division. Dr. Ross concluded over four years in the Army Medical Corps with an assignment to the Surgeon General's Office and as chief of the neurology branch, Neuropsychiatry Consultants' Division.

KENTUCKY

State Association Meeting.—The Kentucky State Medical Association will meet at the Netherland Plaza Hotel, Cincinnati, September 27-30, under the presidency of Dr. Guy Aud, of Louisville. Guest speakers include:

Waltman Walters, Rochester, Minn., Peptic Ulcer.
Robert A. Lyon, Cincinnati, Prophylaxis of Recurrent Rheumatic Fever.
Philip Thorek, Chicago, Early Surgical Diagnosis.
Lloyd F. Zacharias, Cincinnati, Evaluation of Breech Deliveries.
Virgil D. Hauenstein, Cincinnati, Cardiac Emergencies.
George F. Lull, Secretary and General Manager, American Medical Association, Chicago.

The oration in surgery will be given Tuesday noon by Dr. Thomas H. Milton, Owensboro, on "Surgery and Its Relation to the Public," and the oration in medicine Wednesday noon by Dr. George W. Pedigo Jr., Louisville, on "The Clinical Evaluation of Edema."

MARYLAND

Extension of Medical Care to Low Income Groups.—A program of free doctors' care for the poor, administered by the Baltimore city health department with the state defraying expenses, has been initiated. At first benefits, including surgery, dentistry and medicine, will be made available to those on the Welfare Department's relief rolls, but the services will be extended to persons who earn a living but cannot afford to pay medical expenses. Physicians cooperating in the setup will receive $7 a year per patient, regardless of the number of visits made. Services will be given in "medical care clinics" at local hospitals, which receive a flat annual $10 fee per patient cared for. The program is said to have been evolved by the city's medical profession, and, with the exception of the blanket annual fee, is patterned after the medical care system in effect for three years in the twenty-three counties of the state.

Seminars for Health Officers.—A series of seminars in local health administration will be conducted this year to provide regular opportunity for county health officers to discuss their problems. Meetings will be held quarterly in four districts into which the counties have been grouped: north, west, south and east. In each area the quarterly meeting will be conducted by Dr. Ernest L. Stebbins, director of the Johns Hopkins School of Hygiene and Public Health, Baltimore, and Dr. Allen W. Freeman, Baltimore, consultant in public health administration to the state board of health. The program for each session will be formulated by a health officer designated in advance of the meeting, who will prepare and send to the central office an outline of the problems to be discussed. These seminars will not interfere with the annual and quarterly meetings of health officers, bureau chiefs and other personnel that the state department of health has held in Baltimore over a period of years.

MASSACHUSETTS

Board of Registration in Medicine.—At the annual meeting of the Board of Registration in Medicine held July 13, the following officers were elected for the ensuing year: Dr. Gordon M. Morrison, Boston, chairman, and Dr. George L. Schadt, Springfield, secretary. The other members of the board are as follows: Drs. Anthony O. Cardullo, Robert C. Cochrane and Roger T. Doyle, Boston; Charles E. Donovan, D.O., Salem, and Dr. Bancroft C. Wheeler, Worcester.

Research Professor of Medicine.—Dr. Freddy Homburger, associate in the clinical investigation division at the Sloan-Kettering Institute for Cancer Research, New York, has been appointed research professor of medicine at Tufts College Medical School, Boston, to act as head of the cancer research and cancer control units. Dr. Homburger received his medical degree in Switzerland and before joining the Sloan-Kettering staff held fellowships at Harvard Medical School, Boston, and Yale University School of Medicine, New Haven, Conn.

NEBRASKA

Omaha Mid-West Clinical Society.—The Omaha Mid-West Clinical Society's annual assembly will be held at the Hotel Paxton, Omaha, October 25-29. There will be panel discussions on diabetes, gynecology, adolescence, peptic ulcer, antihistaminic drugs, injuries in automobile accidents and the medical expert witness, and a clinicopathologic conference. Among the guest speakers are Morris Fishbein, Richard B. Capps, Oliver E. Van Alyea and Sumner L. Koch, all of Chicago; Benjamin M. Spock and Paul A. O'Leary, Rochester, Minn.; Paul D. White, Boston; James A. Dickson, Cleveland; A. Earl Walker, Baltimore; Charles L. Martin, Dallas, Texas; D. W. Gordon Murray, Toronto, Canada; Robert A. Kimbrough, Philadelphia, and Steven M. Spencer, Swarthmore, Pa.

NEVADA

State Medical Meeting.—The annual meeting of the Nevada State Medical Association will convene at the Hotel Nevada, Ely, September 24-25, under the presidency of Vinton Muller of Reno. Guest speakers include:

Robert G. Weaver, Salt Lake City, Urinary Calculi.
Robert C. Martin, San Francisco, Conditions Commonly Missed in the Ears, Nose and Throat.
Hyrum R. Reichmann, Salt Lake City, Surgical Conditions of the Ano-Rectum.
O. George Bates, San Francisco, Pediatric Problems in General Practice.
Floyd F. Hatch, Salt Lake City, Gastric Surgery.
Frederick C. Cordes, San Francisco, Emergency Treatment of Eye Injuries.
Fletcher B. Taylor, Oakland, Calif., Medical Follies of 1947.
LeRoy C. Abbott and Helen Hagey, San Francisco, Prevention of Deformities in Poliomyelitis.

The council meeting Thursday evening will be addressed by Dr. Joseph C. Bunten, Cheyenne, Wyo. The annual banquet will be Friday evening.

NEW YORK

Regional Diabetes Association.—The Rochester Regional Diabetes Association, has been organized to make the best of medical and nursing care available to all persons with diabetes. The group will function in cooperation with the Rochester Regional Hospital Council with headquarters in the Academy of Medicine. Pamphlets will be distributed and physicians experienced in the treatment of diabetes will be available for lectures and other educational services. Dr. Charles B. F. Gibbs and Dr. H. Raymond Drysdale, both of Rochester, are president and secretary-treasurer, respectively. A board of six physicians will serve as directors of the group.

New York City

Brigadier General Walson to Administer Blood Program.—Brig. General Charles M. Walson, U. S. Army, retired, has been named administrator of the American Red Cross Blood Program of the Greater New York Chapters, 4 East Thirty-Seventh Street. He will direct all phases of the program, which seeks through enrolment of volunteer donors to assure a supply of blood for New York's medical needs. General Walson is a graduate of Jefferson Medical College, Philadelphia, and of the Army Medical School, in 1912. He served in both World Wars.

Survey on Lower East Side.—A survey on the Lower East Side, begun in February 1947 and sponsored by the New York University-Bellevue Medical Center, the New York Heart Association, the city department of health, the Board of Education and the U. S. Public Health Service, showed that 754 children have had rheumatic fever, rheumatic heart disease, congenital heart disease or possible heart disease. Dr. Elvira DeLiee-Burke, research associate in the department of preventive medicine at New York University College of Medicine, is directing the work. Directors of the project plan to extend the survey to the entire city.

OKLAHOMA

Fall Meeting of Clinical Society.—The annual meeting of the Oklahoma City Clinical Society will be held October 25-28 at the Biltmore Hotel, Oklahoma City. The program is made up of a clinical pathologic conference, general assemblies, postgraduate courses, round table luncheons, dinner meetings and commercial exhibits. The registration fee is $15. Guest lecturers will be Drs. Morris Fishbein and John B. Youmans, Chicago; Jerome W. Conn, Ann Arbor, Mich.; Katharine Dodd, Cincinnati; John G. Downing, Boston; Lawrence S. Fallis, Detroit; Arthur B. Hunt and David G. Pugh, Rochester, Minn.; Rudolph H. Kampmeier, Nashville, Tenn.; Frank R. Lock, Winston-Salem, N. C.; William P. Longmire and Allen F. Voshell, Baltimore; Tracy O. Powell, Los Angeles; Harold G. Scheie, Philadelphia; Theodore E. Walsh, St. Louis; Theodore A. Watters, New Orleans, and Owen W. Wangensteen, Minneapolis. Information may be obtained from the Executive Secretary, 512 Medical Arts Building, Oklahoma City.

OREGON

Bone Tumor Registry.—The pathology department at the University of Oregon Medical School, Portland, with the financial assistance of the American Cancer Society, has established a bone tumor registry, to assemble complete case records including the roentgenograms, pathologic material and follow-up data on bone tumor and other bone diseases; to make such material available for study by any qualified doctor of medicine in the state, and to assist physicians in the diagnosis of unusual or obscure bone lesions. Physicians in Oregon are invited to submit completely worked-up cases for the registry. These will be studied by a board of orthopedists, radiologists and pathologists, and reports returned to the submitting physician as early as possible. Cases requiring additional study will be submitted to the Bone Tumor Registry of the Army Institute of Pathology for further opinion. Physicians and surgeons are invited to utilize the study and consultation facilities at any time. The Bone Tumor Registry of the University of Oregon Medical School will supply data to assist the board of health in maintaining statistical records, and it, in turn, will make available to the university and to physicians of the state information gained through maintenance of the registry.

PENNSYLVANIA

Clinical Pathologists Meeting.—The Pennsylvania Association of Clinical Pathologists will hold its fall meeting at the Bellevue-Stratford Hotel, Philadelphia, October 2-3. Papers to be presented will include:

A. Parker Hitchens, Philadelphia, the Clinical Pathologist and the Public Health.
George R. Lacy, Pittsburgh, Survey of the Accuracy of Bacteriologic Examinations in Clinical Laboratories.
Leandro M. Tocantins, Philadelphia, Bone Marrow Biopsy.

There will also be a round table discussion on the training of residents, with Dr. Samuel R. Haythorn, Pittsburgh, as moderator.

Centennial Celebration of State Medical Society.—The Medical Society of the State of Pennsylvania will observe its centennial at the annual meeting at the Bellevue-Stratford Hotel, Philadelphia, October 3-7, under the presidency of Dr. Elmer Hess, Erie. The scientific program will include symposiums on hematology; the thyroid and radioactive isotopes; three "What's New" programs on medicine, surgery and obstetrics and gynecology, and three clinicopathologic conferences. Guest speakers at the general scientific sessions will be:

Stewart G. Wolf Jr., New York, Physiologic Mechanisms of Psychosomatic Phenomena.
Elmer C. Bartels, Boston, An Evaluation of Antithyroid Drugs.
John M. McLean, New York, Corneal Grafting.
Charles C. Dennie, Kansas City, Mo., Man Defends Himself.
Bettina M. Carter, M.S., Pittsburgh, Studies on the Rh Hapten in Relation to Rh Sensitization.
Bradley L. Coley, New York, Early Diagnosis of Tumors of Bone.
Roscoe P. Kandle, New York, Public Health Activities in Pennsylvania.
T. Duckett Jones, New York, Rheumatic Fever and Rheumatic Heart Disease Programs of Care.

The state dinner will be held Monday, and the president's reception Wednesday evening. Besides the technical and scientific exhibit, historical exhibits will show the advancement of medicine. The Woman's Auxiliary will hold its annual meeting beginning October 4 at the Bellevue-Stratford.

VERMONT

Cancer Society Formed.—The Vermont Cancer Society, Inc., was organized last spring as a division of the American Cancer Society under the sponsorship of the Vermont State Medical Society. Dr. Benjamin F. Cook, Rutland, was elected president and Mr. John W. Brownlee, Rutland, secretary. The cancer committee of the Vermont State Medical Society, with Dr. Oscar S. Peterson Jr., Burlington, as chairman, was constituted the medical advisory board of the Vermont Cancer Society.

State Medical Society Meeting.—The annual meeting of the Vermont State Medical Society was held September 15-17 at the Hotel Vermont, Burlington, under the presidency of Dr. Benjamin F. Cook, Rutland. Out of state speakers included:

Richard S. Farr, Syracuse, N. Y., Fractures.
C. Stuart Welch, Boston, Trans-Thoracic Approach for Surgery of the Upper Abdomen.
David S. Grice, Boston, Rationale of Treatment of Acute Poliomyelitis.
Harold T. Hyman, New York, Management of Thrombo-Embolic Disease by the General Practitioner.
Elmer L. Sevringhaus, Nutley, N. J., Use of Endocrines in Functional Bleeding.

At the luncheon meeting on Thursday Dr. Alfred Gellhorn, New York, spoke on "The Red Cross Blood Program." Dr. James R. Miller, Hartford, Conn., trustee, American Medical Association, spoke at the annual banquet on "The World Health Organization, Our Concern in the Health of Other Peoples." Two symposiums were on the program, one on fractured pelves and another on gastroenterology.

VIRGINIA

Establish Department of Legal Medicine.—A department of legal medicine has been added to the Medical College of Virginia curriculum, effective at the beginning of the school term this year. Under the direction of Dr. Herbert S. Breyfogle, Richmond, chief medical examiner of Virginia, the new department will offer courses relating to the collection of scientific evidence for the administration of civil and criminal law and will also engage in research and offer postgraduate work. The first research problem undertaken will be a study of the role of injury in the cause of cancer.

State Medical Meeting.—The Medical Society of Virginia will hold its annual meeting at the John Marshall Hotel, Richmond, October 18-20, under the presidency of Dr. Guy R. Fisher, Staunton. Guest speakers include:

James P. Baker, White Sulphur Springs, W. Va.
Edwin E. Barksdale, Washington, D. C., and George Ellis, Bethesda, Md., Use of the Anti-Histamine Drugs in Dermatology.
Charles S. White, Washington, D. C., Protein Deficiency in Surgical Practice.
Harrison F. Flippin, Philadelphia, Antibiotic and Sulfonamide Therapy.

The banquet will be held Wednesday evening.

GENERAL

Panamerican Convention of Medical Education.—The First Panamerican Convention on Medical Education will be held at the Panamerican Medical Congress in Lima, Peru, December 3-13. The agenda include: (1) report on the status of each respective school of medicine; (2) systems of medical education; (3) the school for postgraduate education; (4) the training and practice of medical specialties, and (5) importance and necessity of research departments.

American Dietetic Association.—The annual meeting of the American Dietetic Association will be held in the Mechanics Building and Hotel Statler, Boston, October 18-22. Sessions will explore results of nutrition research, new methods and technics and progress in community nutrition, diet therapy, food administration and professional education. The program includes a session on new advances in nutrition, another on maternal and child health and two meetings on diet therapy.

Heart Association Employs Fund-Raising Director.—The appointment of Mr. E. J. Ade, technical director for many major war fund drives, as the first fund-raising director of the American Heart Association was announced recently by Dr. Tinsley R. Harrison, president of the association. Mr. Ade will coordinate the activities of national fund-raising committees which are now being established for an expanded 1949 campaign to be climaxed during National Heart Week, beginning next February 14, St. Valentine's Day.

Clinical Congress of Surgeons.—The thirty-fourth Clinical Congress of the American College of Surgeons will be October 18-22, with headquarters at the Biltmore Hotel in Los Angeles. The program of scientific sessions will be supplemented by operative clinics in hospitals, by television and motion pictures, and a four day hospital standardization conference for hospital personnel. Evening symposiums will take up the subjects of cancer, fractures and other traumas, and graduate training in surgery and the surgical specialties. Dr. Clarence M. L. Crafoord, professor of surgery, Karolinska Mediko-Kirurgiska Institutet, Stockholm, Sweden, will deliver the Third Martin Memorial Lecture Monday evening, on "Some Aspects of the Development of Intrathoracic Surgery." The Annual Fracture Oration will be presented by Dr. Henry C. Marble, Boston, on the following evening.

Grants for Study of Multiple Sclerosis.—The National Multiple Sclerosis Society has made grants totaling $77,600 to five medical institutions to conduct medical research projects into the causes and control of multiple sclerosis. Included is a fund to establish the second multiple sclerosis research clinic to be financed by the society, opened August 16 at Albany Hospital, Albany, N. Y. The largest grant will go to Tulane University of Louisiana School of Medicine, New Orleans, to finance a three year study of the possible relation between virus infection and the process of demyelination. A grant was voted to the Massachusetts General Hospital, Boston, for a two year project that will be devoted to basic research in myelin degradation and another to Cedars of Lebanon Hospital, Los Angeles, for an investigation into the behavior of the blood-clotting mechanism in multiple sclerosis. The fifth grant was made to the New York University College of Medicine for a study of psychologic factors in multiple sclerosis.

Incidence of Poliomyelitis.—According to the U. S. Public Health Service, 1,411 cases of poliomyelitis were reported during the week ending August 28, as compared with 1,312 the previous week. Increases of 10 or more cases in the following named states accounted for an aggregate increase of 110 cases (first figure current week, second figure last week): Minnesota 89, 67; Iowa 57, 37; California 226, 206; Texas 71, 54; Michigan 53, 42; New Jersey 50, 40, and Georgia 18, 8. Decreases of 5 or more cases (an aggregate decrease of 83 cases) were reported in the following states: North Carolina 133, 159; New York 87, 99; Florida 5, 14; Tennessee 18, 28; Kentucky 8, 16; Virginia 31, 38; Ohio 76, 82; Wisconsin 31, 36. The increases listed above and those in a few other states resulted in a net increase of 99 cases over the preceding week. Rhode Island continues to be the only state in which no cases have been reported to date. Cases to date total 11,155, as compared with 10,654 in 1946 and a five year median of 5,239 for the corresponding period.

CORRECTIONS

Treatment of Migraine with Histamine.—In the article by this title in THE JOURNAL, July 24, 1948, the dosage on page 1112, column 1, in the fourteenth line from the bottom, should read 0.7 mg. instead of 0.07 mg.

Address of Dr. R. R. Spencer.—The correct address of the author of the article, "The Meaning of Cancer Research," in THE JOURNAL, Aug. 14, 1948, is Dr. R. R. Spencer, United States Public Health Service, National Institute of Health, Bethesda 14, Md. The address of the author given at the end of this article was that of another physician by the same name residing in Chicago.

Marriages

EDGAR COOPER PERSON JR., New York, to Mrs. Mary Elizabeth Altemus Whitney of Upperville, Va., June 18.

JOSEPH BERNARD SHAPSE, Brooklyn, to Miss Constance Reichert Weiss at West Englewood, N. J., May 30.

THOMAS BENJAMIN JOHNSON, Towanda, Pa., to Miss Ruth Elizabeth Casler of Millbrook, N. Y., June 26.

EDMUND A. STEENBERG, Aurora, Neb., to Miss Patricia MacArthur of Schenectady, N. Y., June 23.

GLENN D. VAN GAASBEEK, Kingston, N. Y., to Miss Evelyn Mae Gerhart at Llanerch, Pa., June 26.

EDWARD FINCH PARSONS, Flushing, N. Y., to Miss Elizabeth Platt Hubbell at Garden City, June 25.

DONALD LLOYD GORDON, New York, to Miss Adlynn McKeel Hartley of Englewood, N. J., May 29.

DONALD WALTER MOLINE, Oakland, Calif., to Miss Jacquelin Lee Sharp of Palo Alto, June 19.

WILLIAM LEWIS HALL to Miss Jo Ann Dillon, both of Columbus, Ohio, May 8.

HARVEY HATCHFIELD, New York, to Miss Judith Lang of Brooklyn, March 20.

BENJAMIN H. OREMLAND to Miss Pauline Turchin, both of Brooklyn, June 27.

Deaths

Guy William Wells ✠ Providence, R. I.; born in Springville, Pa., July 9, 1891; Cornell University Medical College, New York, 1920; member of the House of Delegates of the American Medical Association from 1934 to 1937, in 1939, 1940, 1946 and 1947; from 1936 to 1941 secretary of the Rhode Island Medical Society and during 1947 president of the Providence Medical Association; served overseas during World War II; specialist certified by the American Board of Internal Medicine; on the courtesy staff of the Roger Williams General Hospital; on the consulting staffs of the Woonsocket (R. I.) Hospital and Miriam Hospital; on the visiting staff of the Pawtucket (R. I.) Memorial Hospital, where he served as chief of the medical staff; on the staffs of the Providence Lying-In Hospital, South County Hospital, Wakefield, Westerly (R. I.) Hospital, the Charles V. Chapin Hospital and the Rhode Island Hospital, where he died June 15, aged 56, of carcinoma of the stomach.

Taliaferro Clark ✠ Medical Director, U. S. Public Health Service, retired, Germantown, Md.; born in The Plains, Fauquier County, Va., May 14, 1867; University of Virginia Department of Medicine, Charlottesville, 1890; entered the U. S. Public Health Service as an assistant surgeon in 1897; at one time supervised immigration, quarantine and related services in the British Isles and continental Europe; appointed medical director, Assistant Surgeon General in 1930 and acted as chief of the venereal disease division until his retirement in 1933; director of the Child Hygiene Investigation in 1915 and the Bureau of Sanitary Service, American Red Cross from 1917 to 1919; member of the International Sanitation Conference in Paris in 1926; delegate to the International Conference on Tropical Medicine at Cairo, Egypt, in 1928; American member of the Office International d'Hygiene Publique; died in the U. S. Marine Hospital, New York, July 3, aged 81.

Edwin Howe Fiske ✠ Brooklyn; born in Baltimore, Jan. 23, 1877; Long Island College Hospital, Brooklyn, 1901; professor of clinical surgery at the Long Island College of Medicine from 1924 to 1935 when he became emeritus professor; formerly clinical professor of surgery at the University and Bellevue Hospital Medical College in New York; served overseas during World War I; a founder and charter member of the American College of Surgeons; consulting surgeon, Bushwick Hospital, Brooklyn, Eastern Long Island Hospital, Greenport, and Mercy Hospital, Hempstead; served as director of surgery and chairman of the medical board at Kings County Hospital, visiting surgeon at the Hospital of the Holy Family, Midwood and Carson C. Peck Memorial Hospital; died June 16, aged 71.

Henry Pelouze de Forest ✠ New York; born in Fulton, N. Y., in 1864; College of Physicians and Surgeons, medical department of Columbia College, New York, 1890; an Affiliate Fellow of the American Medical Association; formerly adjunct professor of obstetrics at the New York Post-Graduate Medical School and Hospital, Columbia University; veteran of the Spanish-American War; served as sanitary inspector for the city health department, police surgeon, chief medical examiner of the Municipal Civil Service Commission and a member of the medical board of the Teachers' Retirement Board; died June 13, aged 83, of carcinoma of the liver.

Henry Andrews Cotton Jr., ✠ Trenton, N. J.; born in Danvers, Mass., Oct. 14, 1907; Johns Hopkins University School of Medicine, Baltimore, 1934; deputy state commissioner of hospitals; interned at the Johns Hopkins Hospital in Baltimore, where he served a residency; formerly resident at Psychopathic Hospital and Jersey City Hospital in Jersey City and the New Jersey State Hospital in Trenton; served overseas during World War II; member of the American Psychiatric Association; died in the Princeton (N. J.) Hospital, June 21, aged 40, of an accidental overdose of sleeping powder.

Owsley Grant ✠ Louisville, Ky.; born in Louisville in 1887; Johns Hopkins University School of Medicine, Baltimore, 1911; clinical professor of urology at the University of Louisville School of Medicine; specialist certified by the American Board of Urology, Inc.; member of the Southern Surgical Association and the American Urological Association; fellow of the American College of Surgeons; affiliated with the Louisville General, Deaconess, Central State, Baptist and Kosair hospitals and the Norton Memorial Infirmary; died July 1, aged 60, of Banti's disease.

John Merlin Alford ✠ Galva, Ill., Hering Medical College, Chicago, 1908; died April 21, aged 61.

Walter Edward Arnold, Tulsa, Okla.; American Medical College, St. Louis, 1909; died May 1, aged 66.

Ulysses S. Bradley, Harris, Mo.; College of Physicians and Surgeons, Keokuk, Iowa, 1896; died June 21, aged 81, following fracture of the hip.

Charles Brower, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1885; member of the American Medical Association; fellow of the American College of Surgeons; formerly professor of surgery at the University of Nashville Medical Department; served on the staffs of St. Thomas and Nashville General hospitals; died June 24, aged 86, of congestive heart failure.

Robert Ellsworth Brown, Los Angeles; University of Michigan Medical School, Ann Arbor, 1918; served as a medical missionary in China; died May 20, aged 62, of cerebral hemorrhage.

Henry Clay Caldwell, Madison, Wis.; Milwaukee Medical College, 1901; served during World War I; affiliated with the Veteran Administration from 1944 to 1946; died in the Wisconsin General Hospital June 24, aged 73, of cerebrovascular accident and arteriosclerosis.

Richard Henry Carter, Fresno, Calif.; Cooper Medical College, San Francisco, 1895; at one time affiliated with the U. S. Veterans Bureau in San Francisco; served as health officer of Parlier and as assistant county health officer; on the staff of General Hospital of Fresno County; died June 11, aged 77, of heart disease and diabetes mellitus.

John Baptist Casale ✠ Newark, N. J.; Columbia University College of Physicians and Surgeons, New York, 1913; fellow of the International College of Surgeons; president of the medical board and chief of surgery at St. Michael's Hospital; for a short period medical director of the Columbus Hospital; consulting surgeon at American Legion Hospital; died in the Harkness Pavilion of the Presbyterian Medical Center July 8, aged 57, of cirrhosis of the liver.

Weston Percival Chamberlain ✠ Colonel, U. S. Army, retired, Palo Alto, Calif.; Harvard Medical School, Boston, 1897; fellow of the American College of Surgeons; entered the U. S. Army in July 1898; retired June 30, 1935 for disability in line of duty; formerly chief health officer of the Canal Zone; died in Letterman General Hospital, San Francisco, June 7, aged 76, of arteriosclerosis.

Esmond Austin Childs, Long Beach, Calif.; New York Homeopathic Medical College and Flower Hospital, New York, 1909; died in May, aged 67, of coronary thrombosis.

Charles E. Cole ✠ Jacksonville, Ill.; Northwestern University Medical School, Chicago, 1903; veteran of the Spanish-American War; member of the board of the Morgan County Anti-Tuberculosis League; affiliated with Morgan County Tuberculosis Sanatorium "Oaklawn"; died in the Passavant Memorial Hospital May 17, aged 68, of a hip fracture received in a fall.

Metta Viola Collins, Springfield, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; died June 2, aged 82, of bronchopneumonia and arteriosclerotic heart disease.

William John Crotty ✠ East St. Louis, Ill.; St. Louis University School of Medicine, 1919; past president of St. Clair County Medical Society; on the staffs of St. Mary's and Christian Welfare hospitals; president of the State Savings and Loan Association and director of the Southern Illinois National Bank; died May 22, aged 54, of coronary thrombosis.

Ernest Crutcher, Los Angeles; Vanderbilt University School of Medicine, Nashville, Tenn., 1879; died June 1, aged 90, of carcinoma of the prostate.

Edward Cunat, Chicago; Rush Medical College, Chicago, 1900; fell from the fifth floor window of the Presbyterian Hospital April 21, aged 71.

Michael Henry Dalton, St. Louis; Tufts College Medical School, Boston, 1898; member of the American Medical Association; died May 31, aged 80, of cerebral hemorrhage.

Joseph Paul Davis Jr., Turlock, Calif.; University of Oklahoma School of Medicine, Oklahoma City, 1942; member of the American Medical Association; interned at the General Hospital of Fresno County, Fresno; died May 20, aged 33.

Henry Harrison Deen, Leavenworth, Ind.; Hospital College of Medicine, Louisville, Ky., 1906; member of the American Medical Association; county health officer; served during World War I; major, medical reserve corps, U. S. Army; died May 29, aged 72.

William Charles Ehmke, Willow River, Minn.; Minneapolis College of Physicians and Surgeons, 1906; served as mayor and president of the school board; on the staff of the Moose Lake (Minn.) Community Hospital; died May 9, aged 67, of cerebral hemorrhage.

Bruce Bilo Everall, Monona, Iowa; Drake University Medical Department, Des Moines, 1901; member of the American Medical Association; served during World War I; died May 7, aged 69, of coronary thrombosis.

Charles Flett, Milbank, S. D.; Rush Medical College, Chicago, 1895; member of the American Medical Association; for many years member of the county board of health and school board; on the staff of St. Bernard's Providence Hospital; died May 22, aged 82, of uremia.

Penelope McNaughton Flett, Belmont, Mass.; University of Michigan Medical School, Ann Arbor, 1896; served as school physician; died May 3, aged 85, of arteriosclerotic heart disease.

John Francis ✦ Hamilton, Ohio; Miami Medical College, Cincinnati, 1889; died May 25, aged 86.

Francis Augustus Georger, Warrenton, Va.; University of Buffalo School of Medicine, 1913; served during World War I; died May 12, aged 64, of cerebral hemorrhage.

William M. Goodson ✦ Panama City, Fla.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1916; died May 27, aged 54, of coronary thrombosis.

George Henry Griffin, Greensburg, Pa.; Kentucky School of Medicine, Louisville, 1907; served during the Spanish-American War and World War I; on the staff of Westmoreland Hospital; died May 30, aged 69, of carcinoma of the larynx.

Thomas Edward Graham, Charleston, S. C.; Medical College of the State of South Carolina, Charleston, 1907; also a pharmacist; died May 4, aged 65.

E. L. Green, Carpenter, Miss.; Atlanta Medical College, 1895; died in Vicksburg June 25, aged 80.

William David Harvie, Kansas City, Mo.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1889; at one time health officer of Oshkosh, Wis.; served during World War I; died June 1, aged 83, of bronchopneumonia and hematoma of right thigh.

Alfred Hauptmann, Boston; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1905; member of the American Medical Association; specialist certified by the American Board of Psychiatry and Neurology, Inc.; consultant at the Joseph H. Pratt Diagnostic Hospital; died April 5, aged 66, of coronary occlusion.

Maude Ruhl Hill, Cincinnati; Eclectic Medical Institute, Cincinnati, 1894; died in the Holmes Hospital May 18, aged 76.

Samuel Hirsch, Passaic, N. J.; Baltimore University School of Medicine, 1898; member of the American Medical Association; affiliated with Beth Israel Hospital, where he died May 6, aged 71, of coronary sclerosis and diabetes mellitus.

Leon Willet Hyde, Astoria, Ore.; Rush Medical College, Chicago, 1897; veteran of the Spanish-American War; died May 30, aged 74.

J. Sinkler Irvine, Evington, Va.; University of Louisville (Ky.) Medical Department, 1891; member of the American Medical Association; died May 30, aged 81.

George Summers Johnson, Nashville, Tenn.; Washington University School of Medicine, St. Louis, 1925; associate professor of surgery at the Vanderbilt University School of Medicine; member of the Southern Society of Clinical Surgeons; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; served in the medical corps of the U. S. Naval Reserve during World War II; affiliated with the Vanderbilt and Veterans Administration hospitals; died May 20, aged 49, of extradural hemorrhage due to a fall.

Oren Guy Johnson, Mayville, Mich.; Detroit College of Medicine, 1905; member of the American Medical Association; served overseas during World War I; formerly state senator, and mayor of the town of Mayville; on the staff of St. Luke's Hospital in Saginaw; at one time superintendent of the American Legion Children's Billet; died May 19, aged 75, of gangrene of right leg, arteriosclerosis and hypertension.

Ernest Kinloch Johnstone, San Francisco; University of California Medical School, San Francisco, 1892; formerly served in the regular army; died in the Franklin Hospital May 23, aged 77.

Henry William Kleinschmit ✦ Oshkosh, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1914; died May 19, aged 61.

James Archibald Kleinsmid, Phoenix, Ariz.; Rush Medical College, Chicago, 1899; served during World War I; died May 20, aged 71.

Frank Henry Krebs, Philadelphia; Jefferson Medical College of Philadelphia, 1919; died in St. Mary's Hospital May 30, aged 53.

Cary Devall Langhorne, Upperville, Va.; University of Virginia Department of Medicine, Charlottesville, 1897; at one time an officer in the regular navy; veteran of the Spanish-American War; served in the Philippine Insurrection and received a letter of commendation for heroism in action; received the Congressional Medal of Honor for gallantry in action at Vera Cruz during the American Intervention in Mexico; served during World War I; died April 25, aged 74.

Hilliard Lindley, Hollis, Okla.; Southern Medical College, Atlanta, 1891; died April 28, aged 91.

James Thomas Loomis, Long Beach, Calif.; Chicago Physio-Medical College, 1896; at one time practiced in Toledo, Ohio; died May 24, aged 87, of chronic myocarditis.

Herluf Gyde Lund ✦ St. Louis; Washington University School of Medicine, St. Louis, 1907; specialist certified by the American Board of Urology; member of the American Urological Association; affiliated with Lutheran Hospital, where he was chairman of the staff for many years and where he died May 26, aged 65, of multiple abscesses of the kidneys and abscess of the prostate.

Robert James McClure ✦ Calumet, Mich.; University of Michigan Medical School, Ann Arbor, 1933; served as secretary of the Houghton-Baraga-Keweenaw Counties Medical Society and the Upper Peninsula Medical Society; formerly assistant in otolaryngology at the Yale University School of Medicine in New Haven, Conn., and assistant resident otolaryngologist at the New Haven Hospital and New Haven Dispensary; killed in a private plane crash at Laurium May 4, aged 40.

John O. McFerrin, Jasper, Ark.; University of Arkansas School of Medicine, Little Rock, 1905; died in Little Rock May 25, aged 76.

John V. McKim, Bowen, Ill.; St. Louis College of Physicians and Surgeons, 1895; associate member of the staff of St. Mary's Hospital in Quincy, where he died May 24, aged 75, of carcinoma of the colon.

Wade Calhoon Mitchell, Los Angeles (registered in Oklahoma to practice medicine in 1909 and licensed in Kansas in 1901); died April 7, aged 66, of chronic myocarditis and arteriosclerosis.

Salvatore Moncada, Belleville, N. J.; Regia Universita degli Studi di Padova, Facolta di Medicina e Chirurgia, Italy, 1917; member of the American Medical Association; died May 22, aged 56.

Forney Long Murray, American Falls, Idaho; University of Oklahoma School of Medicine, Oklahoma City, 1937; served as director of the South Central District Health Unit in Twin Falls; died May 26, aged 42, of coronary thrombosis.

Rudolph Victor Naumann, New York; New York University College of Medicine, New York, 1942; interned at the Bellevue Hospital, where he served a residency; served a residency at New York and Presbyterian hospitals; certified by the National Board of Medical Examiners; died April 1, aged 39.

Russell Roy Noice, Miami, Ariz.; University of Minnesota Medical School, Minneapolis, 1915; served during World War I; at one time practiced in Minneapolis, where he was county physician; died April 15, aged 57.

William Bryant Oldham, New Castle, Ky.; Hospital College of Medicine, Louisville, 1905; member of the American Medical Association; county health officer; died April 23, aged 66.

Odd V. Opheim ✦ Sioux Falls, S. D.; Rush Medical College, Chicago, 1914; affiliated with the Sioux Valley and McKennan hospitals; died April 29, aged 62, of acute pulmonary edema.

John Green Pittman Jr., Gaffney, S. C.; Medical College of the State of South Carolina, Charleston, 1929; member of the American Medical Association; served during World Wars I and II; died in a hospital at Lancaster May 26, aged 49.

James Norris Plumb, York, Neb.; Rush Medical College, Chicago, 1891; died May 8, aged 80.

Daniel J. Price ✦ Columbus, Ohio; Baltimore Medical College, 1902; died May 8, aged 70.

Samuel Puleston, Sanford, Fla.; University of Maryland School of Medicine, Baltimore, 1902; member of the American Medical Association; died in the Riverside Hospital, Jacksonville, May 28, aged 67, of cardiac hypertrophy and arteriosclerosis.

Ermin Levi Ray, Williamsburg, Mass.; University of Louisville School of Medicine, 1914; served during World War I; affiliated with the Veterans Administration Hospital in Northampton; formerly on the staff of the Veterans Administration Hospital in Lyons, N. J.; died May 21, aged 56, in an airplane accident.

Ralph Clifford Reece, Cincinnati; University of Cincinnati College of Medicine, 1946; interned at the Flower and Fifth Avenue Hospitals in New York and the Cincinnati General Hospital, where he died April 7, aged 26.

Thomas Ludford Rennie, Pell City, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1919; member of the American Medical Association; was burned to death May 8, aged 52.

Charles Henderson Rush, Glendale, Calif.; Cotner University Medical Department, Lincoln, Neb., 1894; died April 24, aged 79, of coronary occlusion.

William Schroeder, Thompson, Iowa; Rush Medical College, Chicago, 1901; died May 29, aged 72, of diabetes mellitus.

Mattie Brown Shaw, Ashland, Ore.; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1897; died April 6, aged 74.

Lewis Mayer Shultz, Port Carbon, Pa.; Medico-Chirurgical College of Philadelphia, 1916; served overseas during World War I; died May 30, aged 54, of uremia.

Henry Franklin Smith, Chattanooga, Tenn.; Memphis Hospital Medical College, 1913; died in the Erlanger Hospital May 2, aged 61, of cerebral embolus.

Arthur A. Snyder, McLean, Va.; University of the City of New York Medical Department, New York, 1882; for many years practiced in Washington, D. C., where he was on the staff of the Garfield Memorial Hospital; veteran of the Spanish-American War; died May 15, aged 88.

Floyd Rodman Stamp, Alliance, Ohio; Tufts College Medical School, Boston, 1912; member of the American Medical Association; served as county health commissioner for many years; died April 27, aged 66.

John Henry Taylor Jr., Trenton, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1927; on the staff of the New Jersey State Hospital, where he died May 2, aged 46, of acute nephritis.

Victor Clifford Tisdal ✠ Elk City, Okla.; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1910; past president of the Oklahoma State Medical Association; veteran of World War I; served as mayor of Elk City and member of the state board of health; formerly owner of the Tisdal Hospital; died in the University Hospital, Oklahoma City, May 18, aged 62, of coronary thrombosis.

Francis Lewis Tribon, Algona, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1893; died May 23, aged 84, of chronic myocarditis.

Luther Brown Turner, Columbus, Ohio; Starling Medical College, Columbus, 1892; on the staff of the Mercy Hospital, where he died April 23, aged 85.

Nellie Smith Vernon, Astoria, Ore.; University of Oregon Medical School, Portland, 1901; served as city and county health officer; died in Portland May 23, aged 80.

KILLED IN ACTION

CAPT. LOUIS COWEN
M. C., A. U. S., 1908-1945

LIEUT. COL. DAN. B. SEARCY
M. C., U. S. Army, 1909-1945

CAPT. ALEXANDER A. ST. CLAIR,
M.C., A.U.S., 1911-1945

Louis Cowen, New York; University of Buffalo School of Medicine, 1935; interned at the Trinity Hospital in Brooklyn; member of the American Medical Association; began active duty as a first lieutenant in the Medical Corps, Army of the United States, in May 1941; promoted to captain; killed in action in Germany March 1, 1945, aged 37.

Dan Beville Searcy ✠ Lieutenant Colonel, M. C., U. S. Army, Lewisville, Ark.; born in Lewisville, Ark., Feb. 12, 1909; Tulane University of Louisiana School of Medicine, New Orleans, 1934; interned at the Shreveport Charity Hospital in Shreveport, La.; commissioned a first lieutenant in the Medical Corps of the U. S. Army on Dec. 1, 1938; transferred to the Air Corps and sent to Carlisle Barracks after graduating from Aviation School of Medicine at Randolph Field, Texas; completed a course for flight surgeons at Walter Reed General Hospital in 1941, was sent to the Philippine area at the fall of Bataan; served in Australia and New Guinea; promoted to lieutenant colonel in December 1942; received the Legion of Merit for services at Del Monte, Mindanao, Philippine Islands, from Dec. 1, 1941 to April 29, 1942; missing in action since Jan. 18, 1943; declared dead as of Dec. 20, 1945, aged 36.

Alexander Armstrong St. Clair, Bluefield, W. Va.; University of Virginia Department of Medicine, Charlottesville, 1936; member of the American Medical Association; interned at the Lankenau Hospital and Children's Hospital of the Mary J. Drexel Home in Philadelphia; later studied surgery in Austria and Hungary; received a certificate from the University of Vienna in the theory and practice of surgery; on the staff of the Bluefield Sanitarium; began active duty as a lieutenant in the medical corps, Army of the United States on Feb. 11, 1941; promoted to captain; reported missing in action since July 13, 1943 on a flight from Mohanbari Air Base, India, to Kunming, China; determined dead Dec. 19, 1945, aged 34.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 4, 1948.

World Federation for Mental Health

The formation of a World Federation for Mental Health to act in close collaboration with the specialized agencies of the United Nations was announced at a session of the International Congress on Mental Health in London. Membership of the federation is open to organizations whose object is the promotion of mental health and human relations. About one hundred and fifty delegates representing forty-two nations and four colonial territories are responsible for its formation. Dr. J. R. Rees, president of the International Commission for Mental Hygiene, was elected first president of the federation, and Dr. André Repond, of Switzerland, vice president. Dr. Rees was neurologic specialist to the Ministry of Pensions and during the war was consulting psychiatrist to the Army. He is a well known writer on psychiatry.

Physicians Elected Fellows of Royal Society

The highest scientific distinction in this country is the Fellowship of the Royal Society, which is awarded only for original important scientific work. In the case of physicians the recipients are generally workers in experimental subjects, such as physiology and biochemistry, and only very eminent clinicans are so honored. The following members of the medical profession have been elected: Dr. R. A. McCance, professor of experimental medicine in the University of Cambridge, for his contributions to metabolic studies in man; Sir Leonard Parsons, emeritus professor of diseases of children in the University of Birmingham, for his studies in child health and the wasting disorders of children; Dr. W. A. H. Rushton, lecturer in physiology in the University of Cambridge, for his researches on the effects of electrical stimuli on muscles and nerves.

The Prevention of Venereal Disease

The latest report of the Ministry of Health shows an increase during 1945 in the incidence of gonorrhea and syphilis. In a letter to the medical press Lord Horder, president of the National Society for the Prevention of Venereal Disease, points out that this has happened in spite of the expenditure of large sums by the government, through the Central Council for Health Education, in telling the public of the dangers of venereal disease, coupled with treatment after the disease has developed. But the public has not been allowed to learn the important fact that much of the disease is easily prevented. During the great wars the fighting services all over the world, owing mainly to the persistent efforts of the society, were protected (more or less, according to the enthusiasm of the officer in charge) against these diseases by the preventive measures which the society has advocated for thirty years. But all the time the civilian population has been kept in ignorance and hence the increase. The policy of the society is threefold: (1) to educate the public with regard to the fact that disease can be prevented by simple scientific measures; (2) to supply details of such measures, and (3) to secure alteration in the law to enable preventive means to be sold with the necessary instructions.

Lord Horder's letter has provoked dissenting replies in the *British Medical Journal*. It is stated that during the war some medical officers, who pressed prophylactic measures by every means at their disposal, were driven to the conclusion that they had not diminished but increased the rate of infection, because such advocacy increased sexual promiscuity. A venereologist of extensive experience in the Army and Navy, and to a less extent in a large civilian clinic, has found prophylactic measures futile. The secretary of the Association for Moral and Social Hygiene insists that the only sure preventive is chastity and that any propaganda which obscures this fact is likely to increase promiscuity and hence to increase the dissemination of venereal disease. The armed forces have had for many years easy access to prophylactic packets and are instructed in their use; yet the incidence of venereal disease is always a great worry to the authorities. The troops occupying Germany are instructed in prophylaxis; yet the incidence of venereal disease was 185 per thousand in 1947. It is suggested that these troops are largely responsible for the spread of venereal disease in our civil population.

PARIS

(From Our Regular Correspondent)

July 30, 1948.

First International B.C.G. Congress

This Congress, which was held at the Paris Pasteur Institute, under the presidency of Dr. G. Guérin, was attended by delegates from almost every nation. More than one hundred communications were read before the four sections.

To the first section was entrusted the experimental study of B.C.G. and of the methods of its administration. Researches on the preparation of B.C.G. in its dry state have been simultaneously undertaken by Ungar and Muggleton (Great Britain), Rosenthal (United States), Kaiser (Austria) and Bretay (France). By his method for desiccating the vaccine at a low temperature, the latter has obtained a powder of B.C.G. keeping for months the vitality of the germs. Among other things, the preventive action of B.C.G. has been demonstrated by the experimental works of E. Bernard and Kreis, who found that guinea pigs previously vaccinated and superinfected with virulent Koch's bacilli respond better to streptomycin than the nonvaccinated ones. In the second section, dealing with the results of the use of B.C.G. in human beings, various methods of vaccination were discussed: Rosenthal's method (United States) of multiple punctures; Negre and Bretay's one of scarifications, especially used in France, and the intradermal route of Wallgren, preferred in Scandinavian countries. Professor Debre reported that in collaboration with the World Health Organisation and the International Fund for the Relief of Infancy a "pilot station" is being created in Paris for the systematic study of the differences between the various technics of vaccination. This station will also be of use for the instruction of doctors and nurses. The work of the third section concerned the results obtained with B.C.G. in veterinary practice. It has been proved that B.C.G. vaccination on a large scale could largely diminish the extension of tuberculosis in cattle; for instance, in France, where 40 per cent of the cattle are tuberculin positive. The fourth section dealt with the conditions of application of B.C.G. in the field of preventive hygiene. Tonell reported the results of vaccination in a Swedish district of 100,000 inhabitants. Thanks to systematic vaccination in primary and secondary schools (18,000 vaccinations) from 1935 to 1946, no tuberculous meningitis has been observed in this district, and the mortality rate, which was 6 per 10,000 up to 1939, decreased to 2.6 per 10,000 in 1946. As emphasized by Wallgren and Guilbaux, the vaccinated patient must be kept free from contagious contacts for several months in order to realize immunization.

The congress then passed unanimously, among others, the following resolutions: that over ten million vaccinations practiced in the whole world for twenty-five years confirm the absolute innocuity of B.C.G. vaccination in human beings; that B.C.G. vaccination constitutes the most effective means of preventing tuberculosis; that the vaccine B.C.G. strain used in all countries originates from the Paris Pasteur Institute; that the technic confirmed by tests in Paris at the Pasteur Institute insures its vitality; that the congress recommends the introduction of the vaccine through the skin, the modes of applica-

tion of which are varied; that the congress does not exclude the oral administration for practical reasons; that the congress recommends the revaccination of subjects whose cutaneous sensitivity to tuberculin has disappeared; that the congress considers urgent as widespread a diffusion as possible of the B.C.G. vaccination; that the congress recommends the development of all other prophylactic measures employed in the fight against tuberculosis.

TURKEY

(From Our Regular Correspondent)

ANKARA, Aug. 16, 1948.

Streptomycin in Tuberculous Meningitis

Not until the middle of 1947 was it possible to obtain streptomycin for the treatment of tuberculous meningitis. The price was 15 Turkish pounds or $4.80 for 1 Gm., but within a few months the black market was selling it for $9.00, and as a result during June and July 1948 no streptomycin was available at the Istanbul, the Izmir or the Ankara pharmacy. During the war years tuberculosis greatly increased; hence the government recently granted $250,000 for the purchase of American streptomycin. In view of the scarcity of the drug, its distribution is at present under the supervision of the Ministry of Health. Health officers are responsible for its distribution in the provinces.

Prof. Dr. Ihsan Hilmi Alantar of the Istanbul Children's Hospital reports on the use of streptomycin in 19 cases of tuberculous meningitis. All 19 children belonged to well to do parents who had been able to procure the new drug. Eight of the 19 patients were girls and 11 were boys; their ages ranged from 2 to 12 years. In 18 of the patients another form of tuberculosis was concomitant with meningitis. The clinical diagnosis in all 19 patients was verified by the tuberculin test, test of the cerebrospinal fluid, or the inoculation of animals. In all 19 patients the albumin content of the cerebrospinal fluid had risen. The Pandy test elicited a clearly positive reaction, and the lymphocytes ranged from 12 to 640 per cubic millimeter. Löwenstein cultures were positive in 3 cases. Of the 11 animals inoculated 3 contracted tuberculosis. Of the 19 patients some received a total of 15 to 20 and others from 50 to 120 Gm. of streptomycin; several of the latter are still under treatment. The patients received an average daily dosage of 1 Gm. of streptomycin; older children and those with the most serious cases 2 Gm. of streptomycin, this dosage being continued as long as possible. Intramuscularly and intrarhachidian routes were used; the daily dosage given by the intrarhachidian route was 0.1 to 1.5 Gm. In several cases the therapy had to be abandoned temporarily because the children could no longer bear the repeated injections, or when complications like severe headaches, vomiting, excitement or insomnia arose. There were intervals of two weeks to more than two months. Edema, redness and swelling at the point of injection appeared in almost all 19 patients, especially in extremely small children, requiring a change of injection point. There were several infiltrations and one sterile abscess; in 3 patients urticaria appeared; no true nephritis was observed, but in 3 cases albuminuria. The streptomycin affected the vision of 11 patients. In many papillary stasis occurred; in 5 of the latter greatly weakened visual perception replaced the papillary stasis, so that in one 18 month old child complete atrophy of the visual nerve occurred. The streptomycin therapy was discontinued and the patient was given a large dosage (3.025 Gm.) of vitamin B_1 injection, and the vision returned. In 1 patient symptoms of mastoiditis developed toward the end of the therapy. In several patients whose condition on admission was grave cerebral paralysis soon developed, and in several others it developed later. Of the 19 patients 5 fully recovered; 2 patients are still under treatment with hope of full recovery, and 12 patients whose condition on admission was very serious did not recover.

BELGIUM

(From Our Regular Correspondent)

Aug. 7, 1948.

Medical Meetings at Brussels

More than five hundred physicians and surgeons of Belgium, France, Great Britain, United States, Switzerland, Holland, Luxemburg, Portugal, Greece, Italy, Czechoslovakia, Iran, Canada and the Dominican Republic convened in Brussels for the twenty-second session.

The success was due to the cooperation of the scientific societies in arranging their meetings to coincide with the medical meetings. There are to be mentioned the International Association of Medical Electronics, the Meetings on Dentistry, the extraordinary session of the Belgian Medical Society on Physical Education and Sports, the extraordinary session of the Belgian Society of Scientific Studies on Tuberculosis and Pneumonology, of the Belgium Society Against Rheumatism and the extraordinary session of the Medicosurgical Section of the National Society of the Belgian Railroads.

Among numerous scientific reports presented were the following: Is Intelligence Electronic? by Professor Dacos; Ideas Relating to Physical and Biologic Electronics, by Professor Rylandt, who was inclined to connect his data to chronaxia; Biology of Physical Training, by Professor Pierre Combemale; Special Indications for Streptomycin in the Course of the Treatment of the Tertiary Forms of Pulmonary Tuberculosis in the Adult, by Dr. Jeanneret; The Resuscitation of the Heart, by Professor Mercier Fauteux; Observations on Carcinoma of the Lung, by Dr. C. Price Thomas; The Destructive Effect of Microwaves in Biology: Can They be Employed as War Weapons? by Dr. Victor Tomberg; Recent Progress in Chemotherapy of Cancer, by Dr. Alexander Haddow.

Finally, a conference was held by General Sicé, professor of tropical pathology at the University of Basel. It is said that General Sicé plays an important role in the approach of the Tchad (French colony in the African Sudan) and Equatorial Africa to the Free French Forces. He also assumed the difficult task of sanitary organization of the African campaign for these forces. He spoke on the combat of dehydration and dechloridation as the result of extreme heat.

International Union of Railroad Physicians

The National Society of Belgian Railroads has organized under the auspices of Dr. Huybrechts at a scientific session, during which the medical chiefs of the great networks of France, Holland, Switzerland and England with the Council of Administration prepared the way for an international union of railroad physicians. The following passages are from the paper presented by M. Verbist, Minister of Public Health, who epitomized the tendencies with regard to the organization of medicine in Belgium:

> It is with good reason that physicians defend, under all circumstances, liberty of choice and professional secrecy as the essential conditions of the practice of their art. Without liberty of choosing the physician, the nurse and the institution of medicosocial care or assistance, there is no longer any truly humane medicine. Our constant care in all regulations which we take is to reconcile the requirements of technic and those of liberty.
>
> We are convinced that to ameliorate everywhere the health and well-being is the first and the most important contribution which one can make today to social peace. As long as men and women and children die of hunger in the world or are struck down by disease and destitution all desperation and all catastrophes are possible and civilization is menaced. It is generosity and fraternity between peoples which can save a dangerously troubled world. Efficiently to preserve the health and well-being of human beings is to safeguard peace.

National Exhibit of Physician Artists

The third National Exhibit of physician painters organized by the Circle of Art and Medicine with the collaboration of the Belgian Chemical Society was opened at Brussels. It has been said that this is a curious exhibit of distinguished amateurs. More than twenty painters and sculptors have combined their works in the beautiful rooms of the Artists' Circle of Brussels. Many of these amateurs have shown serious qualities, and it is interesting to see this movement develop year after year.

Council on Medical Service

RÉSUMÉ OF ACTIVITIES OF CONSTITUENT ASSOCIATIONS AND COMPONENT SOCIETIES

A preliminary survey has been made of state association and county society activities which may serve as a basis for compiling more detailed information in the future, particularly on organization activities as they refer to the National Health Program of the American Medical Association.

Constituent Associations

Following is a brief résumé of replies received from 45 of the 53 constituent medical associations, which consist of 48 state medical associations, the District of Columbia and the four territorial medical associations. For the purpose of simplicity, the terms constituent and state are used interchangeably in this résumé.

Committees To Work With Council On Medical Service.—Direct contact with the state medical associations is recognized as a necessity by the Council. In fact, soon after completing its organization, the Council requested each state association to appoint a committee, either new or existing, to work with the Council. These committees were then invited to meet with the Council—usually five or six states meeting together in some central place. In this manner the regional conferences of the Council on Medical Service were started. Their purpose is to learn of the views and problems of the state medical associations and present to them the views and problems of the American Medical Association. Of the 45 state associations answering the questionnaire 31 have committees to work with the Council on Medical Service.

Organization.—The first state medical association to organize formally was the Medical Society of New Jersey (1766); the most recent was the Alaska Territorial Medical Association (1925). Fourteen were organized prior to the formation of the American Medical Association. The number of associations organized during the Civil War period (1851-1875) is greater than during any other twenty-five year period.

A majority (39) of the associations are corporations, incorporated under state or territorial laws. Incorporation has definite advantages for a medical organization, particularly when its activities extend beyond the purely academic field, when it holds or owns property and when it has a sizeable budget and operating personnel.

While almost every state medical association has a house of delegates composed of physicians selected by the component medical societies, to carry out the legislative decisions most associations have a smaller group elected by the house of delegates. The range in the number of members on these governing boards is from 5 to 21, with about one half of the associations (26) having boards of less than 15 members.

All of the 45 associations, excepting Alaska, reported having at least one part time employee; all but 7 have full time employees. A total of 333 persons are on association payrolls, of whom 270 are full time and 63 are part time.

Membership.—Membership in constituent medical associations, except for the territories and the District of Columbia, is dependent on membership in the component county or district medical societies. Physicians do not join either the constituent medical associations or the American Medical Association; they join the county medical society and are "certified" to the state, which, in turn, reports them to the American Medical Association. The 45 state associations answering the questionnaire reported memberships ranging from 43 (Alaska) to 21,786 (New York). Only 13 have less than 1,000 members, while 7 have a membership of more than 5,000.

Annual dues paid by state association members range from $5 in Mississippi to $60 in California. In general, however, the dues are rather low compared to other organizations to which physicians belong, a majority being less than $25 a year. Each state association seems to set its dues to provide sufficient income to meet its own idea of necessary activity. With one exception, the 7 associations with over 5,000 members have annual budgets of over $100,000. Those in the 2,500 to 5,000 membership group seem to require a minimum budget of $50,000 annually. In associations of less than 2,500 members, no general requirement is evident.

Scientific Activities.—In promoting scientific education in the field of medicine, the state associations continue to fulfil their proper function.

As one activity in this field, 36 state medical associations publish scientific journals. In addition, 11 others participate with one or more associations in publishing a journal. In every instance these journals are devoted primarily to scientific medicine, although most of them publish official actions of the association, news notes from the component county societies and papers or items on social medicine.

Of the 45 associations reporting, 34 provide or make postgraduate programs available for their members. Three are organizing or are in the process of organizing postgraduate programs.

Professional and Public Relations.—The state medical associations are recognizing more and more the need for a planned public relations program to explain the achievements of medicine to the public. Twenty-nine associations reported a public relations program in operation, and 3 are in the process of organizing one. Although these are public relations programs, much of the activity is directed toward physicians; to a considerable extent, then, they are also professional relations programs. In fact, several associations are concentrating on contacts with the profession in order to lay the groundwork for future activity in the field of public relations.

The secretaries' conference has been a regular activity of several state associations for many years. More recently, however, the National Conference of County Medical Society Officers has directed an increased attention toward this particular activity. At present 18 state associations sponsor a secretaries' conference, thus indicating a growing awareness of the need for indoctrinating the officers of the component county medical societies.

News letters are becoming popular among the state medical associations. When the Council on Medical Service began publishing its *News Letter* five years ago, only a few state associations were using this medium to keep in touch with their members. Fourteen now publish regular news letters.

A speakers' bureau can be an important activity, bolstering the scientific programs of the county societies as well as serving the public. That this activity has not been explored to its limit is shown by the fact that only 16 associations reported such a bureau in operation, while 3 reported one in process.

The widespread interest in health councils has not had any particular effect on the formation of state health councils. Twenty state associations report participation in health councils, most of which have been in operation for several years. An additional 4 associations reported health councils in process.

Over one half of the state health councils are limited to representatives of the various professions: medicine, dentistry, pharmacy, etc. In this they differ from the popular conception of a health council, which is composed of representatives of all groups, professional and lay.

Component Societies

For the purpose of tabulation the replies from the county societies have been divided into two groups. Group I refers to replies received from county medical societies having a regular headquarters office and employing lay personnel. Group II refers to replies received from societies which do not employ lay personnel. Tabulation of the information received has been made as brief as possible. The names of specific county societies have been omitted in the tabulation of various activities, but will be made available to physicians or society executives on request.

Organization.—Eleven societies reported owning their own building; in addition, one society is raising funds for a building, and another is considering a building program. Other societies in group I are housed as follows: 36 rent offices and 18 use other facilities, such as hospitals and medical libraries.

Sixty-seven of the 159 societies replying employ lay personnel, and they are in 29 of the 48 states. In 52 of these societies the

lay personnel is listed as full time and in 15 as part time. Some are full time executive secretaries; others are librarians, and a few are listed as part time secretaries. Thirty-six employees listed as executive secretaries are men, and approximately 20 are women.

A few counties in group II have offices, most of them requiring space only for their scientific meetings. However, 6 state that they rent offices; one owns its own building; one has plans under way for building its own headquarters, and another indicated that funds were being accumulated for a building program.

Considering the functions and responsibilities of the county societies, it is surprising how much is accomplished with so little in funds. While the annual dues range from nothing to $50, almost 60 per cent of the 159 societies reporting collect $15 a year or less per member. The average physician pays more than this for a day of recreation.

Scientific Activities.—The scientific meeting is one of the county medical society's important functions. Most county medical societies were organized for the purpose of providing their members with an opportunity to keep pace with the scientific medical advancements, and 115 of the 159 societies reporting have a monthly meeting schedule.

While county medical societies continue to sponsor regular scientific meetings, the declining attendance at such meetings is an unsolved problem. The increasing number of hospital meetings, easy transportation to medical centers and the pressure on the physicians by outside sources all contributed to the reduction of attendance at the county society programs. The Council asked the questions "What topics draw best" and "What topics draw least." In answer to the first question a majority of the societies in both groups I and II stated that "general medical programs of interest to general practitioners" draw the best attendance. In answer to the second question, an equally large majority in both groups answered that papers on "specialty subjects" or "nonmedical subjects" draw the least. Other programs listed as well attended are those presenting "recent advances in medicine" and conducted by "well known guest speakers." "Research papers" and "local speakers" were not popular to the general membership.

In addition to the regular scientific meetings, many county societies have organized or make available special postgraduate programs for their members. In group I, 36 societies reported that postgraduate programs were available to the members. In group II, 38 societies reported that postgraduate programs were available to the membership.

The availability of medical library facilities is most important to the present day physician. As a result, most of the medical societies serving the larger cities have either developed their own medical libraries or have made provision for the use of medical library facilities on the part of their membership. Of the 67 county societies reporting in group I, 24 have their own libraries and 32 state that facilities are available to their members. The replies show that physicians in the smaller communities also have library facilities available to them. Of the 92 societies in group II reporting, 15 have their own libraries and 42 have other medical library facilities available to their members.

Other Activities.—Following is a tabulation of other activities carried on by the medical societies in both group I and group II.

Activity	Number of Societies Group I	Group II
Health councils	46	36
Indigent care programs	37	28
Cancer detection programs	47	59
Tuberculosis case finding programs	39	47
Bulletins	55	49
Radio programs	38	11
Speaker's bureau	38	28
Collection bureaus	23	8
Telephone answering services	28	29
Blood bank	23	12
Insurance-Malpractice	31	40
Accident and health	41	50
Life	4	6
Annuities	—	2
Social Activities		
Parties	51	63
Golf tournaments	31	27
Bowling league	7	5
Other	18	16

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Ruptured Blood Vessel in Eye Due to Strain.—This was an action for the recovery of a workmen's compensation award for an eye injury which occurred during the course of the petitioner's employment. From the granting of an award, the employer appealed to the Supreme Court of Oklahoma.

The petitioner was employed as a tool dresser in a well-drilling operation. While lifting a heavy beam of about 100 pounds a dark spot suddenly developed in his left eye, which nearly blinded him. It subsequently developed that the strain of lifting had so increased his blood pressure as to cause the rupture of a blood vessel in his eye, with the result that he became industrially blind. The petitioner's eye specialist admitted that an existing tubercular condition had weakened the walls of the blood vessels in the eye, but he stated definitely that the injury was due to the lifting of the beam.

The employer contended that the strain of lifting the beam was not an unusual or extraordinary strain, but was an ordinary occurrence in connection with the petitioner's work and that therefore the petitioner did not sustain an accidental injury as that term has been defined by other decisions of the Supreme Court of Oklahoma. The court, however, pointed out that the term "accident" as employed in the compensation acts is broad enough to include an injury from muscular strain or physical overexertion, such as hernia, or rupture, or bursting blood vessels, even though the physical condition of the employee is such as to predispose him to the injury. In the instant case, the Supreme Court continued, the evidence sufficiently showed a strain which, according to the testimony of the petitioner's physician, led directly to the hemorrhage in his eye. The strain of lifting the beam, while lifting was frequently undertaken by the petitioner, was not what could be termed an ordinary occurrence. We have frequently held, the Supreme Court concluded, that an injury occasioned by a strain which causes a dormant or latent condition to light up is an accidental injury within the workmen's compensation act. Accordingly the award in favor of the petitioner was sustained.—*Special Indemnity Fund v. McFee, 193 P. (2d) 301 (Okla., 1948).*

Medical Motion Pictures

FILM REVIEW

Trichomonal and Monilial Vaginitis, Pathology—Diagnosis—Treatment. 16 mm., color, sound, 1,500 feet, (1 reel), showing time forty-one minutes. Prepared in 1947 by J. P. Greenhill, M.D., Cook County Hospital, Chicago. Produced by the Medical Film Guild, New York through a grant from the G. D. Searle & Co., Chicago. Procurable on loan from The Medical Film Guild, 167 West Fifty-Seventh Street, New York 19.

The film presents with considerable detail an outline of the diagnosis and treatment of trichomonal vaginitis. Included are a discussion of laboratory diagnostic procedures and several scenes depicting an ancient aspect of part of the history of vaginal infection. The latter could be omitted, as the scenes tend to detract from the main subject of the film.

The photography is good except for the photomicrographs. The narration is not undertaken by a professional. Some criticism can be directed at the length of the film, as lengthiness encourages unnecessary details. The diagnosis and treatment of trichomonal vaginitis may not always be as simple as depicted in the film, nor is the percentage of cases probably as high as indicated. Furthermore, the danger of contamination from the rectum by the method of wiping the anus, as well as the comparatively uncommon symptoms, general weakness and malaise, has been overemphasized. Air embolism might occur after the use of the demonstrated squirting device. While other criticisms are indicated the film does offer information that the general practitioner may welcome. It will not be especially suitable for the classroom in medical schools because of its length and limited discussion.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I & II.* Various Centers, Feb., June, and Sept., 1949. *Part II.* April, 1949. Exec. Sec., Mr. E. S. Elwood, 225 S. 15th St., Philadelphia 2, Pa. *Part III.* Boston & New York, Autumn. Sec., Dr. J. S. Rodman, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various Centers, Jan. 21, 1949. Final date for filing application is Oct. 1. *Oral,* Philadelphia, Oct. 10. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 18. *Oral.* Chicago, Oct. 13-15; Philadelphia, Nov. 3-5; San Francisco, date not set. Candidates not taking these special oral examinations will have no opportunity for admission next year. Sec., Dr. W. A. Werrell, 1 W. Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, June 1949. Final date for filing application is Jan. 1949. Sec., Dr. W. J. German, 310 Cedar Street, New Haven, Conn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I.* Various Centers, Feb. 4, 1949. Final date for filing application is Nov. 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 1.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Chicago, Oct. 6. *Written.* St. Louis, Oct. 15-19. Sec., Dr. S. J. Beach, 56 Ivie Rd., Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPEDIC SURGERY: *Part I.* Various Centers, April & May. Final date for filing application is Dec. 31. Sec., Dr. Francis M. McKeever, 1136 W. 6th St., Los Angeles 14.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-8. New York City, Spring, 1949. Sec., Dr. D. M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 8-9. Final date for filing application is Oct. 1. Sec., Dr. Robert A. Moore, 507 Euclid Ave., St. Louis.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Atlantic City, Nov. 17-19. Sec., Dr. Lee F. Hill, 718 Royal Union Bldg., Des Moines, Iowa.

AMERICAN BOARD OF PLASTIC SURGERY: Examinations are given in June and November of each year in the home town of applicants. Sec., Treas., Dr. Louis T. Byars, 400 Metropolitan Bldg., St. Louis, Mo.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 13-15. Sec., Dr. F. J. Braceland, 102-110 Second Ave., S., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, March 1949. Final date for filing application is Dec. 1. Sec., Dr. J. S. Rodman 225 S. 15th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 28-30, 1949. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

ARKANSAS: * Little Rock, Nov. 4-5. Sec., Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Eclectic Examination.* Little Rock, Nov. 4. Sec., Dr. C. H. Young, 1415 Main St. Little Rock.

CALIFORNIA: *Oral.* Los Angeles, Nov. 20-21. *Written.* Sacramento, Oct. 18-21. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

COLORADO: * *Endorsement.* Denver, Oct. 5. Final date for filing application is Sept. 18. Sec.-Treas., Dr. Walter W. King, 831 Republic Bldg., Denver 2.

CONNECTICUT: * *Examination.* Hartford, Nov. 9-10. Sec., Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic Examination.* Derby, Nov. 9-10. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

FLORIDA: * *Examination.* Jacksonville, Nov. 28-30. Sec., Dr. Frank D. Gray, 12 N. Rosalind Ave., Orlando.

GEORGIA: *Examination.* Atlanta, Oct. 12-13. *Endorsement.* Atlanta, Oct. 14. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: *Endorsement.* Agana, Last Friday of each month. Sec., Capt. C. K. Youngkin, Dept. of Public Health, Guam, % F.P.O. San Francisco, Calif.

IDAHO: Boise, Jan. 19-12. Dir., Bureau of Occupational Licenses, Miss Estella S. Mulliner, State House, Boise.

ILLINOIS: Chicago, Oct. 5-7. Supt., Dept. of Registration and Education, Mr. Fred W. Ruegg, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June 1949. Sec., Board of Medical Registration & Examination, Dr. Paul R. Tindall, 416 K. of P. Bldg., Indianapolis.

IOWA: * *Examination.* Des Moines, Dec. 6-8, *Endorsement.* Des Moines, Oct. 4. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Topeka, Dec. 15-16. Sec., Board of Medical Registration & Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 13-15. Sec., Dr. Bruce Underwood, 620 S. 3rd St., Louisville 2.

LOUISIANA: *Examination.* New Orleans, Dec. Sec.-Treas., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans 12. *Homeopathic Examination.* Baton Rouge, subject to call. Sec., Dr. F. H. Hardenstein, 715 Pere Marquette Bldg., New Orleans.

MAINE: Portland, Nov. 9-10. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, Dec. 14-17. *Endorsement.* At the discretion of the Board. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. *Homeopathic Examination.* Baltimore, Dec. 7-8. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: *Examination.* Boston, Nov. 16-19. Sec., Board of Registration in Medicine, Dr. G. L. Schadt, 413 E. State House, Boston.

MICHIGAN: * *Examination.* Lansing, Oct. 13-15. *Endorsement.* Oct. 12. Sec., Dr. J. E. McIntyre, 203 Hollister Bldg., Lansing.

MINNESOTA: Minneapolis, Oct. 19-21. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Reciprocity.* Jackson, Dec. 6. Exec. Officer, State Board of Health, Dr. Felix J. Underwood, Jackson.

MISSOURI: St. Louis, Oct. 25-27. Exec. Sec., Mr. John A. Hailey, P.O. Box 4, Jefferson City, Mo.

MONTANA: Helena, Oct. 4-6. Sec., Dr. O. G. Klein, First Nat'l Bank Bldg., Helena.

NEVADA: Carson City, Nov. 1. Sec., Dr. G. H. Ross, Industrial Bldg., Carson City.

NEW JERSEY: *Examination.* Trenton, Oct. 19-22. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * Santa Fe, Oct. 11-12. Sec., Dr. V. E. Berchtold, 141 Palace Ave., Santa Fe.

NEW YORK: *Examination.* Various Centers, Sept. 27-30. Sec., Dr. J. L. Lochner, Jr., 23 South Pearl St., Albany 7.

OHIO: *Examination.* Columbus, Dec. *Endorsement.* Columbus, Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: * *Reciprocity.* Oklahoma City, Oct. 24-25. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: * *Examination.* Portland, Jan. 1949. *Endorsement.* Oct. 15-16. Final date for filing application is Oct. 1. Exec. Sec., Mr. Howard I. Bobbitt, 608 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia, Jan., 1949. Act. Sec., Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

RHODE ISLAND: * *Examination.* Providence, Oct. 7-8. Chief, Div. of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Endorsement.* Oct. 4. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA: * Pierre, Jan. 18-19. Sec., Dr. G. J. Van Heuvelen, Capitol Bldg., Pierre.

TENNESSEE: * Memphis, Sept. 29-30. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

TEXAS: Fort Worth, Nov. 4-6. Sec.-Treas., Dr. M. H. Crabb, Medical Arts Bldg., Fort Worth.

UTAH: *Examination.* Salt Lake City, July. *Endorsement.* Oct. 4. Sec., Dept. of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.

VERMONT: *Examination.* Burlington, Feb. Sec., Dr. F. J. Lawliss, Richford.

VIRGIN ISLANDS: *Examination.* Charlotte Amalie, Dec. 8-9. Comm., Dr. Christian R. Moorhead, Charlotte Amalie.

VIRGINIA: *Examination.* Richmond, Dec. 3-4. *Endorsement.* Dec. 2. Sec., Dr. K. D. Graves, 30½ Franklin Road, Roanoke.

WASHINGTON: * Seattle, Jan. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WEST VIRGINIA: Charleston, Oct. 4-6. Comm., Public Health Council, Dr. N. H. Dyer, State Dept. of Health, Charleston.

WISCONSIN: * Madison, Jan. 11-13, 1949. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls, Wis.

WYOMING: *Examination.* Cheyenne, Oct. 4. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination.* Tucson, Sept. 21. Sec., Mr. Francis A. Roy, Univ. of Arizona, Tucson.

ARKANSAS: *Examination.* Little Rock, Oct. 5. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

CONNECTICUT: *Examination.* Oct. 9. Exec. Asst., Mary G. Reynolds, 110 Whitney Ave., New Haven 10.

DISTRICT OF COLUMBIA: *Examination.* Washington, Oct. 18-19. Sec., Dr. G. C. Ruhland, 4130 Municipal Bldg., Washington, D. C.

FLORIDA: *Examination.* Gainesville, Nov. 6. Final date for filing application is Oct. 25. Mr. M. W. Emmel, University of Florida, Gainesville.

IOWA: Des Moines, Oct. 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MICHIGAN: *Examination.* Ann Arbor and Detroit, Oct. 8-9. Sec., Miss Eloise LeBeau, 1510 West Allegan St., Lansing.

MINNESOTA: *Examination.* Oct. 5-6. Sec.-Treas., Dr. Raymond N. Bieter, 105 Millard Hall, Univ. of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, Oct. 5-6. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, Room 1009 State Capitol Bldg., Lincoln.

NEW MEXICO: *Examination.* Santa Fe, Sept. 19. Sec., Miss Marguerite Kilkenny, 110 W. Houghton St., Santa Fe.

OKLAHOMA: Spring of 1949. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Dec. Sec., Basic Science Examining Committee, Dr. C. D. Byrne, Univ. of Oregon, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 3-4. Sec., Dr. G. M. Evans, Yankton.

TENNESSEE: *Examination.* Memphis & Nashville, Sept. 20-21. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

WASHINGTON: Seattle, Jan. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WISCONSIN: *Examination.* Madison, Sept. 25. Final date for filing application is Sept. 18. Sec., Prof. W. H. Barber, Scott & Watson Sts., Ripon.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

18:349-450 (May) 1948

Green Pastures in Pathology. S. P. Reimann.—p. 349.
Isotopes in Medicine. Grace Medes.—p. 354.
Kahn Reactions with Cardiolipin Antigen Compared with Kahn Antigen. II: Note on Microflocculation Procedure with Cardiolipin Antigen. R. L. Kahn and Elizabeth B. McDermott.—p. 364.
Isoimmunization with the A and B Factors and Its Relation to Hemolytic Disease of Newborn. S. H. Polayes and J. McNally Jr. —p. 375.
Growth of Pathogenic Fungi on New Culture Medium. M. L. Littman. —p. 409.
Plasma Concentrations Following Intramuscular Injections of Various Doses of Penicillin. A. Kathrine Miller and W. P. Boger.—p. 421.
Effect of Variations in Concentration of Non-Protein Constituents of Serum on Correlation Between Specific Gravity and Protein Content. R. A. Mortensen.—p. 429.
Simple Method of Determining Nonprotein Nitrogen, Total Protein and Albumin in Blood Serum Samples by Using Conway Cells. S. Levy. —p. 435.
Application of Weichselbaum Biuret Reagent to Determination of Spinal Fluid Protein. M. Ditterbrandt.—p. 439.

American Journal of Medicine, New York

4:1-626 (April) 1948. **Partial Index**

Pneumonia and Erythema Multiforme Exudativum: Report of 4 cases and 3 Autopsies. M. Finland, L. S. Jolliffe and F. Parker Jr. —p. 473.
Differential Diagnostic Problems in Acute Pulmonary Embolization. I. R. Roth.—p. 493.
*Origin of Thirst in Diabetes Insipidus. J. H. Holmes and M. I. Gregersen.—p. 503.
Radiation Injuries of Intestines. C. W. Hock, J. Rodrigues, Anna Hamann and W. L. Palmer.—p. 511.
Lichen Planus, Atypical: Report of 10 Cases. A. A. Holbrook.—p. 525.
Neurogenic Pain Simulating Visceral Disease. L. Motley.—p. 539.
Treatment of Hypertensive Vascular Disease with Rice Diet. W. Kempner.—p. 545.
*Low Salt Diets and Arterial Hypertension. H. A. Schroeder.—p. 578.

Thirst in Diabetes Insipidus. — Holmes and Gregersen studied 5 cases of diabetes insipidus in order to evaluate the mechanism of polydipsia under the following conditions: (1) water ad libitum, (2) pitressin therapy, (3) the forcing of fluids and (4) ingestion of salt. During intense thirst there was a reduction of salivary flow. When thirst was abolished by pitressin therapy or by the forcing of fluids, the salivary flow increased to normal values. These observations are consistent with the "dry mouth" theory of thirst. Pitressin therapy or the forcing of fluids resulted in an increase in plasma volume and extracellular volume over the values observed for untreated diabetes insipidus. The thirst mechanism in diabetes insipidus is similar to that observed in simple dehydration and is caused in this instance by the severe polyuria. This is confirmed by the observations that pitressin therapy or the forcing of fluids alleviates thirst and produces increases in plasma and extracellular volume and in salivary flow similar to that observed after ingestion of water in dehydration. Salt, while it may be effective in maintaining plasma volume and available fluid at the same levels as observed under pitressin therapy and when fluids are forced, does not abolish the thirst of diabetes insipidus; on the contrary, it increases the polydipsia. The reaction to salt is the same as that seen in the normal person.

Low Salt Diets in Hypertension. — Schroeder discusses some of the difficulties in the use of low salt diets in the management of hypertension. The possible role of the adrenal cortex in arterial hypertension and its relation to disturbances in tension and its relation to disturbances in salt balance are considered in the light of experimental and clinical evidence. While many subjects respond favorably to rigid restriction of salt by lowering of blood pressure, psychotherapeutic influences may play a large part in this change in some. If subjects are adequately controlled, the change to be expected is not great and may be absent in patients with severe hypertension in whom therapy is most needed. It is possible that patients who do respond favorably to this diet exhibit a different type of hypertension in which the adrenal cortex is overactive. The mechanism of the response is not understood. No special advantage has been demonstrated in the use of a diet exclusively composed of rice, fruit juices and vitamins, as compared with a normal diet with a similar content of salt, and this diet has several disadvantages.

American J. Obstetrics and Gynecology, St. Louis

55:367-550 (March) 1948. **Partial Index**

Plasma Proteins in Pregnancy. J. L. Macarthur.—p. 382.
Study of Maternal Mortality in Canada. Marion Kerr.—p. 396.
Vaginal Repair Combined with Vaginal Hysterectomy. J. E. Harrison.—p. 403.
Sterility in the Female. K. M. Grant.—p. 416.
Improved Operative Technic for Salpingostomy. H. W. Johnston. —p. 426.
Study of Breech Delivery. A. E. Trites.—p. 430.
*In Vitro Fertilization and Cleavage of Human Ovarian Eggs. Miriam F. Menkin and J. Rock.—p. 440.
Evaluation of Vaginal Smear Method for Diagnosis of Uterine Cancer. L. C. Scheffey, A. E. Rakoff and J. Hoffman.—p. 453.
*Observations on Vaginal Absorption of Penicillin. S. Abel, C. J. Farmer and Jeanne Doucette.—p. 461.
Permeability of Human Placenta to Sodium in Normal and Abnormal Pregnancies and Supply of Sodium to Human Fetus as Determined with Radioactive Sodium. L. B. Flexner, D. B. Cowie, L. M. Hellman and others.—p. 469.
Fate of Living Viable Babies in Extrauterine Pregnancies. M. Suter and C. Wichser.—p. 489.
Antepartum Hemorrhage. R. A. Kimbrough and B. D. Jones.—p. 496.
Elective Use of Kielland Forceps in Management of Occipitoposterior and Occipitotransverse Positions. L. M. Miles.—p. 504.
Multiple Sulfonamide Therapeutic Measure in Postoperative Care of Cervix and Vagina. A. H. Marbach.—p. 511.
Anemias of Pregnancy. P. J. Talso and W. J. Dieckmann.—p. 518.
Antenatal Blood Group Determination. Preliminary Report. S. H. Polayes, S. Lubin and J. McNally Jr.—p. 524.
Late Recurrence of Cervical Carcinoma Following Radiation Therapy. H. Speert.—p. 533.

In Vitro Fertilization of Human Eggs. — Menkin and Rock performed in vitro insemination experiments with human eggs. Fertilization was obtained and cleavage induced in three experiments. The eggs were recovered from ovarian tissue removed from 3 women between the ages of 31 and 38 years on whom complete hysterectomy and right salpingo-oophorectomy were performed on the tenth, the eleventh and the twelfth day of the cycle. The eggs were obtained from follicles of the extirpated ovary, one to four and one-half hours following oophorectomy. After rapid transfer through three portions of sterile Locke's solution, the eggs were pipetted into a Carrel flask containing 3 cc. of serum prepared from the blood of the egg donor. The eggs were then placed in the incubator at 37.5 C. After an incubation period of twenty-two and one-half to twenty-seven hours the eggs were rapidly transferred through small amounts of Locke's solution in three watch glasses. In the third watch glass were then pipetted a few drops of a suspension of spermatozoa which had been at room temperature for two hours and forty-five minutes to four and one-half hours after ejaculation. The watch glass containing the ovum and spermatozoa was observed for one hour under the microscope. The spermatozoa were clearly seen to travel through the interstices of the loose cellular formation surrounding the egg, and many were noted in active motion around the pellucid zone. That was followed by culture of the preparation in human blood serum for forty and one-half hours to forty-six hours. When examined at the end of the incubation period two of the eggs were found to be in the two-cell stage, and two in the three-cell stage. The time relations in these experiments are in general accord with those reported previously for the in vivo fertilized tubal monkey egg cultured in vitro, as well as for in vivo fertilized mouse eggs studied at different intervals after copulation.

Vaginal Absorption of Penicillin.—Abel and his co-workers studied the absorption of penicillin calcium from the vagina in 39 women who were divided in four groups in whom blood level studies were conducted. In 10 patients between the ages of 23 and 59 years, who had vaginitis, 100,000 units of penicillin

was inserted vaginally prior to the blood level studies. In 5 additional patients with vaginitis between the ages of 23 and 59 years, 200,000 units of penicillin was inserted vaginally. Five hospital clinic patients between the ages of 39 and 60 years who were free of vaginal abnormalities were given 200,000 units of penicillin vaginally. The last group consisted of 19 single hospital nurses between the ages of 22 and 34 years whose blood levels were studied following the vaginal insertion of 200,000 units of penicillin. The degree of absorption and the resulting blood penicillin level were subject to great variation. They are difficult to predict in any given case. Apparently there is less absorption of penicillin from the normal vaginal mucosa than from the inflamed mucous membrane in patients with vaginitis. Because of the incidence of side reactions (2 of the nurses had urticaria during the study) and, because of the unpredictable blood levels obtained subsequent to the use of penicillin vaginal suppositories, it does not seem rational to advocate this route of administration in preference to intramuscular injection or oral therapy when the desired result is the production and maintenance of a therapeutic blood penicillin level. The real value of penicillin vaginal suppositories is in the treatment of vaginitis when the local concentration of penicillin is of prime importance and the production of blood levels is a matter of secondary interest.

American Journal of Ophthalmology, Cincinnati

31:387-526 (April) 1948

Some Confusing Factors in Diagnosis of Paralysis of Vertically Acting Muscles. F. H. Adler.—p. 387.
Problem of Sympathetic Ophthalmia. B. Samuels.—p. 397.
Simple Ptosis Operation: Utilization of Frontalis by Means of Single Rhomboid-Shaped Suture. J. S. Friedenwald and J. S. Guyton. —p. 411.
Visual-Field Interpretations in Chiasmal Lesions. D. Kravitz.—p. 415.
Relationships Between Lateral Heterophoria, Prism Vergence and Near Point of Convergence. R. G. Scobee and E. L. Green.—p. 427.
*Discoloration of Eyelids from Prolonged Use of Ointments Containing Mercury. M. Wheeler.—p. 441.
Use of Buccal Mucosa in Restoration of Orbital Socket. J. N. Greear Jr. —p. 445.
Angiosarcoma of Orbit. P. V. Carelli and J. P. Cangelosi.—p. 453.
Discussion of Deformities of Shape of Lens, with Report of Case of Posterior Lenticonus. W. B. Doherty.—p. 457.

Discoloration of Eyelids from Mercury.—Wheeler reports 5 patients with a characteristic dirty gray discoloration of the skin of the eyelids. These cases have one point in common; namely, daily use of an ophthalmic ointment containing mercury (yellow oxide or ammoniated) over a prolonged period, four years being the shortest. There appears to be a direct etiologic relationship between the mercury and the pigmentation. The color fades slowly after use of the ointment has been discontinued.

American Journal of Public Health, New York

38:467-612 (April) 1948

The Health Officer's Bookshelf. H. Williams.—p. 467.
Current Status of Immunization Procedures. R. S. Muckenfuss.—p. 476.
Quaternary Ammonium Compounds in Sanitization. E. C. McCulloch, S. Hauge and H. Migaki.—p. 493.
Factors Affecting the Properties of Quaternary Ammonium Compounds as Sanitizers. G. M. Ridenour and E. H. Armbruster.—p. 504.
Eradication of Tuberculosis by Epidemiologic Methods. J. A. Myers. —p. 516.
Relationship of Tryptophane to Incidence of Dental Caries. N. C. Turner and G. E. Crowell.—p. 525.
Pattern of Industrial Hygiene in the United States. W. T. Ingram. —p. 534.
*Paralytic Shellfish Poisoning on Canadian Atlantic Coast. J. Gibbard and J. Naubert.—p. 550.

Shellfish Poisoning.—Gibbard and Naubert say that in 1936 Canadian public health officials realized that there was a mussel poisoning problem in Canada when in Nova Scotia 5 cases with 2 deaths occurred after consumption of mussels. Inquiries conducted in the Maritime Provinces revealed that there have been many unrecorded outbreaks. Residents of fishing communities know of the dangers of eating poisonous mussels. They have acquired food habits that afford protection. They will eat only the adductor muscle of the scallops. Surveys have been conducted since 1943 to determine the danger season, the dangerous areas and the dangerous species of shellfish. The clinical picture was studied in 28 cases. The symptoms, varying in severity with the amount of poison ingested, were: numbness about face and mouth, "pins and needles" feeling about the lips, vomiting, headache, dizziness, difficulty in breathing, general weakness and occasional paralysis. The ultimate source of the poison has been shown to be in a species of dinoflagellate Gonyaulax tamarensis, one of the planktonic organisms on which the shellfish feed. The appearance of high toxicities and large numbers of the dinoflagellate have been simultaneous, that is, between mid-July and the end of September. The process of canning as it is practiced commercially reduces the poison content of clams to safe levels. Commercial packs are sampled when the toxicity of clam fishing grounds rises. The scallop industry presents no problem, since the adductor muscle, the only part marketed, has been demonstrated to be consistently free of poison.

38:613-760 (May) 1948

Developments in Use of Newer Organic Insecticides of Public Health Importance. J. M. Andrews and S. W. Simmons.—p. 613.
Is Rh Factor a Public Health Laboratory Function? Anna I. Van Saun. —p. 632.
Blood Grouping and Rh Typing in State Public Health Laboratory. R. A. MacCready and R. T. McGee.—p. 637.
Production and Proper Use of Rh Typing Reagents. L. K. Diamond. —p. 645.
Human Waste Disposal from Railroad Passenger Cars. A. Wolman and L. K. Clark.—p. 652.
Essentials for Control of Ragweed. I. Weinstein and A. H. Fletcher. —p. 664.
Comparative Efficiency of Rectal Swabs and Fecal Specimens in Detecting Typhoid and Salmonella Cases and Carriers. H. J. Shaughnesy, F. Friewer and Adele Snyder.—p. 670.
Susceptibility to Typhus of Rats on Deficient Diets. Florence K. Fitzpatrick.—p. 676.
Epidemiology of Rheumatic Fever; Its Public Health Aspects. G. C. Griffith.—p. 682.
General Reactions of Mothers and Nurses to Rooming-in: Observations Based on Experience in Four Bed Rooming-in Unit in Grace-New Haven Community Hospital. Edith B. Jackson.—p. 689.
Can Public Health Agencies Handle Poliomyelitis Alone? H. E. Van Riper.—p. 696.
Coördination of Hospitals and Health Departments. E. D. Barnett, J. W. Mountin and others.—p. 700.

Am. J. Roentgenol. and Rad. Therapy, Springfield, Ill.

59:469-616 (April) 1948

*Effects of Radioactive Sodium on Leukemia and Allied Diseases: Preliminary Report. T. C. Evans, M. Lenz, C. P. Donlan and M. J. LeMay.—p. 469.
Experimental Studies on Motility of Gastric Mucosa in Dogs: Preliminary Report. F. P. Brooks, L. W. Stevens, E. P. Pendergrass and F. Bassols.—p. 482.
Primary Tumors of Small Intestine. C. C. Dundon.—p. 492.
Cavernous Hemangioma of Frontal Bone with Report of Case of Sinus Pericranii. M. H. Poppel, J. F. Roach and H. Hamlin. —p. 505.
Atlanto-Occipital Fusion, Ossiculum Terminale and Occipital Vertebra as Related to Basilar Impression with Neurologic Symptoms. L. A. Hadley.—p. 511.
Important Sequelae and Complications of Hemothorax Resulting from Penetrating Wounds of Pleural Cavity. S. P. Barden.—p. 525.
Multiple Congenital Malformations of Skeletal System: Case Report. E. J. Gordon, N. Shechter and A. W. Perlman.—p. 533.
Dental Aids in Treatment of Cancer of Head and Neck. A. J. Ackerman.—p. 539.
*Roentgen Treatment of Cancer of Esophagus. J. R. Freid.—p. 551.

Radioactive Sodium in Leukemia.—Evans and his co-workers started their investigations with radiosodium in 1944. Since then 31 patients have been treated, and in 24 enough information has been gained to permit a few tentative conclusions. They gained the impression that it is an effective means of giving protracted whole body irradiation. Radiation has produced good results in a few patients. The method appears to be adaptable to chronic myelogenous leukemia, chronic lymphatic leukemia, polycythemia vera and other radiosensitive generalized diseases. The response to radiosodium therapy is not good when (1) the disease is acute, (2) the radioresistance of the abnormal cells is high and (3) the hemopoietic system is already damaged. The rapidity and degree of response, as well as the duration of the regression, can usually be regulated by the amount of each radiosodium dose and the frequency of treatment. It has been possible to obtain satisfactory responses with radiosodium without producing radiation sickness. Some slight nausea for a few days followed heavy and frequent treatment in 2 patients. The radiosodium was given by mouth as a solution of sodium chloride. This method of administration avoids some of the complications and limitations of intravenous injec-

tion as used by some. The use of radiosodium will probably not become widespread, as it is limited to laboratories near the source of supply. Its half-life is only about fifteen hours.

Roentgen Treatment of Cancer of Esophagus.—Fried relates experiences with radiation therapy of cancer of the esophagus. Radium treatment has been largely abandoned and roentgen therapy is the method of choice. On the basis of experiences at Montefiore Hospital with radiation treatment, survival in months appears to have been increased for those patients who were treated. In 4 cases necropsies were performed some time after irradiation; 3 showed no evidence of carcinoma, and in the fourth case only a few degenerating cells were found. One patient from the author's private practice is living and well seven years and seven months following irradiation. The author discusses the complications associated with intensive irradiation.

American Journal of Surgery, New York

75:643-756 (May) 1948

Treatment of Fractures of Long Bones by Open Reduction and Screw Fixation: Report of 42 Cases. H. G. Lee.—p. 645.
Etiology of Goiter in Man: New Concepts. C. B. DeCourcy and J. L. DeCourcy.—p. 661.
Current Reappraisal of Total Abdominal Hysterectory. W. J. Reich and M. J. Nechtow.—p. 670.
Repair of Fascial Defects with Whole Skin Grafts. W. A. Swanker. —p. 677.
Simplified Technic for Subtotal Thyroidectomy. U. Maes, L. Kuker and C. Craighead.—p. 683.
Management of Recurrent Varicose Veins. L. K. Stalker.—p. 688.
Procidentia: New Operation to Cure "Remaining" Prolapsed Cervix or Vaginal Hernia. R. C. Chaffin.—p. 691.
Use of Curare in Anesthetic Management of Profoundly Sedated Patient. Edith Eason and Mary Karp.—p. 695.
Anterior Dislocation of Elbow with Fracture of Olecranon. L. H. Strug.—p. 700.
Middle Meningeal Hemorrhage. H. A. Shenkin and F. C. Grant.—p. 704.
Mucocele of Appendix. A. Behrend.—p. 709.
Glossopharyngeal Nerve Block. E. A. Rovenstine and E. M. Papper. —p. 713.
Congenital Chondrosternal Depression (Funnel Chest) Relieved by Chondrosternoplasty. H. A. Brodkin.—p. 716.
Gastric Resection for Duodenal Ulcer: Surgical Treatment and Follow Up Study. H. L. Skinner and R. D. Duncan.—p. 721.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

32:203-300 (May) 1948

Bismuth Plus Penicillin in Treatment of Experimental Syphilis. H. J. Magnuson and Barbara J. Rosenau.—p. 203.
Penicillin Verus Penicillin-Malaria in Treatment of Dementia Paralytica. Y. T. Wong and H. Packer.—p. 212.
Serologic Response in Penicillin-Treated Symptomatic Neurosyphilis. J. P. Scully, M. S. Falk and J. H. Stokes.—p. 224.
*Treatment Failures Following Use of Penicillin in Late Syphilis. F. W. Reynolds.—p. 233.
Gummatous Osteomyelitis with Pathologic Fracture Complicating General Paresis. E. G. Olmstead.—p. 243.
Electrophoretic Analysis of Serum from Patients with Pinta and Yaws. M. L. Dillon and G. R. Cooper.—p. 251.
Venereal Disease in Prostitutes. T. Rosenthal and G. Kerchner. —p. 256.
Alleged Penicillin-Resistant Gonorrhea. R. P. Hughes and C. M. Carpenter.—p. 265.
Value of Roentgenography of Male Urethra Following Infection. M. L. Brodny and S. A. Robins.—p. 272.
Simultaneous Herpes Zoster and Lymphogranuloma Venereum. L. Gardner.—p. 286.
Virulence and Antigenicity of Hemophilus Ducreyi. R. B. Dienst. —p. 289.

Failure of Penicillin in Late Syphilis.—The Venereal Disease Division of the Medical Clinic of the Johns Hopkins Hospital has participated in the nationwide study of penicillin in syphilis, and thus far approximately 550 patients with various late manifestations of the disease have been treated with penicillin. Reynolds points out that treatment failures following the use of penicillin in late syphilis occur as a result of (1) drug resistance, (2) clinical progression, (3) recurrence of lesions following an initially favorable response and (4) the subsequent development of new manifestations of syphilis elsewhere in the body. That a significant number have occurred within the relatively brief period of clinical use of penicillin should be a matter of concern to all who use penicillin in the treatment of syphilis. Theoretic considerations suggest that penicillin ultimately may prove to be less efficacious against Tryponema pallidum in the later stages of syphilitic infection than during the more acute early phases of the disease. He advises caution in the use of penicillin as the only therapeutic agent in the treatment of late syphilis.

American Practitioner, Philadelphia

2:497-566 (April) 1948. **Partial Index**

*Observations on Treatment of Subacute Bacterial Endocarditis with Penicillin and Streptomycin. H. R. Pearsall, R. P. Pillow and J. E. Wood Jr.—p. 497.
Some Practical Considerations in Management of Obesity. R. C. Rothenberg.—p. 507.
Sternal Puncture. L. R. Limarzi.—p. 514.
Neurosyphilis. R. H. Kampmeier.—p. 523.
The Use of Sulfadiazine-Sulfathiazole Mixture Combined with Systemic Alkalizers. L. Oettinger Jr. and G. Cronheim.—p. 526.
*The Treatment of Human Anthrax with Penicillin. L. Weinstein and Charles S. Oliver.—p. 533.

Penicillin and Streptomycin in Subacute Bacterial Endocarditis.—The 19 patients with subacute bacterial endocarditis whose cases are reviewed by Pearsall and his associates received treatment with penicillin, and some were given streptomycin as well. Twelve of the 19 patients have been able to resume a fairly normal existence and may be regarded as cured. Inability to obtain bacteriologic arrest was seen in only 3 cases. Five of the 7 deaths were due primarily to congestive failure secondary to severe valvular damage. Penicillin is still the drug of choice in the treatment of this disease, but streptomycin saved the lives of 2 patients after the failure of penicillin. In vitro resistance of bacteria to penicillin is not necessarily an unfavorable sign. Bacterial arrest with penicillin was accomplished in several patients in the face of reported penicillin resistance. In vivo response to antibiotic administration is the final test in bacterial resistance. Enhancement of penicillin levels with caronamide and related drugs offers new hope in the management of certain patients with bacterial endocarditis.

Treatment of Anthrax with Penicillin.—Weinstein and Oliver report 3 cases of cutaneous anthrax in men who worked at occupations where they came in contact with hides or wool. One sustained a scratch while unloading Argentinian hides, and the other 2 worked in carpet and rug factories where they had contact with wool. In one instance the lesion was on the face; in another on the neck, and in the third there were two malignant pustules on the right forearm. Bacteremia occurred in the person who had the two lesions; he was also found to have Bacillus anthracis in the spinal fluid during an acute episode of disorientation. All 3 patients were given penicillin intramuscularly and all made a complete recovery. The response to treatment with penicillin appeared to be more rapid than that attributed to the sulfonamide compounds, antiserum, or when these agents were used alone or in various combinations. Since the mortality rate of cutaneous anthrax is only about 16 to 22 per cent, it is difficult to evaluate the importance of penicillin in saving the lives of the 3 patients. Because of lack of toxicity as compared with the sulfonamide compounds, antiserum and neoarsphenamine and the rapidity with which clinical improvement takes place, penicillin appears to be the agent of choice in the treatment of cutaneous anthrax.

American Review of Tuberculosis, New York

57:311-432 (April) 1948. **Partial Index**

Virus Pneumonia. M. D. Eaton.—p. 311.
Prophylactic Immunization and Specific Therapy of Experimental Pneumonic Plague. K. F. Meyer, S. F. Quan and A. Larson.—p. 312.
*Actinomyces in Chronic Bronchopulmonary Infections. E. B. Kay. —p. 322.
Use of Coccidioidin. C. E. Smith, E. G. Whiting, E. E. Baker and others.—p. 330.
Histoplasmosis and Pulmonary Calcifications. J. C. Peterson and A. Christie.—p. 361.
Fatal Coccidioidomycosis: Case of Laboratory Infection. D. T. Smith and E. R. Harrell Jr.—p. 368.
Heart Disease Detection in Preemployment Examinations. B. E. Kuechle.—p. 383.
Age Specific Susceptibility to Tuberculosis: Experiments on Guinea Pigs and Rats. C. J. Duca.—p. 389.
Acid-Base Condition in Tuberculosis. H. S. Kolmer, D. Ellis, T. Smith and others.—p. 400.
Tuberculous Laryngitis: A Controlled Study. J. P. M. Black.—p. 409.

Actinomyces in Chronic Bronchopulmonary Infections.—Kay maintains that the frequency with which diagnosis of pulmonary actinomycosis is made depends on the frequency with which one requests a bacteriologic examination for Actinomyces, the amount of exudate provided, the experience of the bacteriologist and the care exercised in culturing methods. During one period of six months at the Chest Center at Kennedy

General Hospital during the war, Actinomyces organisms were isolated from the sputum in 109 of 240 patients. They were also isolated from exudate obtained bronchoscopically in 65 of these 109 patients. The exudate aspirated from pulmonary abscesses in 6 patients, and from the sinus tracts of 2 patients, also contained Actinomyces in combination with other organisms. Thirty-seven of the 65 patients with Actinomyces organisms in bronchial exudate had bronchiectasis with varying degrees of pneumonitis. The Actinomyces organisms in patients with bronchiectasis were felt to be saprophytic and not clinically important under aerobic conditions. In another 8 patients the only apparent disease was a moderately severe chronic bronchitis. There was roentgen and clinical evidence of either aspiration pneumonia, pulmonary abscess or extensive pulmonary suppuration in 20 patients. Actinomyces was isolated and cultured from these patients from exudate obtained bronchoscopically or aspirated from pulmonary abscesses, and in 6 instances taken directly from the lung after pulmonary resection. The finding of Actinomyces with such frequency caused considerable concern. Care was exercised to verify the identity of this supposedly pathogenic non-acid-fast anaerobic ray fungus. Sputum is an unreliable source for examinations for fungous infections because of the contamination by the bacterial flora of the mouth. The author discusses the response to conservative and surgical therapy and says that the prognosis depends largely on the severity of the infection. Favorable response occurred with the use of chemotherapeutic drugs and antibiotics, particularly when these were used in conjunction with surgical therapy. In 9 patients healing resulted only after resection of the diseased pulmonary tissue by lobectomy or pneumonectomy.

Annals of Allergy, Minneapolis

6:99-218 (March-April) 1948

Electroencephalograms of Allergic Children. Susan C. Dees and H. Lowenbach.—p. 99.
Experimental Studies on Acute Disseminated Encephalomyelitis in Rhesus Monkey.—p. 109.
Psychosomatic Aspects of Hay Fever and Asthma Prior to 1900. H. A. Abramson.—p. 110.
Effects of Decapryn Succinate, a New Antihistamine Agent, in Some Natural and Acquired Hypersensitivities in Animals. Barbara B. Brown and H. W. Werner.—p. 122.
Studies on Eggwhite Sensitivity in Rat: Influence of Endocrine Glands. J. Leger and G. M. C. Masson.—p. 131.
Vulvo-Vaginal Pruritus Associated with Hay Fever. W. F. Mitchell, Iola Sivon and J. H. Mitchell.—p. 144.
Temporal Arteritis: Case Report. M. Zeller.—p. 148.
Convulsions Following Epinephrine: Report of Case. A. Seltzer.—p. 151.
Weltmann Reaction in Allergic Rhinitis. Susan C. Dees and D. J. Vracin.—p. 154.

Annals of Otol., Rhin. and Laryngology, St. Louis

57:5-282 (March) 1948. **Partial Index**

Orbital Complications Resulting from Lesions of Sinuses. A. T. Smith and J. T. Spencer.—p. 5.
Observations on Bone Conduction in Fenestration Cases: Physiologic Considerations. A. L. Juers.—p. 28.
Reevaluation of Implantation of Fascial Strips Through Masseter Muscle for Surgical Correction of Fascial Paralysis: Report of Three Additional Cases. N. Owens.—p. 55.
Special Technic for Diagnosis and Treatment of Psychogenic Deafness. W. G. Hardy.—p. 65.
Influenzal Laryngitis. D. W. Brewer and J. H. Tom Rambo.—p. 96.
*Treatment of Chronic Nasal Diphtheria Carriers: Report of Case. J. X. Medwick and O. E. Hallberg.—p. 134.
Laryngeal Edema in Epidemic Parotitis. J. S. Walker and E. L. Gann.—p. 163.
Penicillin Treatment of Nerve Deafness Due to Syphilis. W. E. Loch and H. A. Tucker.—p. 167.
Relation of Dosage to Streptomycin Toxicity. R. Tompsett.—p. 181.

Treatment of Nasal Diphtheria Carriers.—Medwick and Hallberg report the case of a man, aged 71, who was seen at the Mayo Clinic in June 1947. He complained that he had a bad throat and that he had been found to be a diphtheria carrier in March 1945, after routine culture of material from the nose and throat at a state hospital in which he was employed. Symptoms included a purulent nasal discharge and variable degrees of irritation of the throat for a few years prior to his coming to the clinic. The patient never had been immunized against diphtheria. At the age of 7 years he had had diphtheria. Nasal polyps had been removed, first in 1924 and seven times subsequently. Measures adopted by the patient to alter his status as a carrier of diphtheria included the persistent local application of various antiseptic agents and sprays for two years, without success. Because of the chronic sinusitis, intranasal surgical treatment combined with the use of penicillin and diphtheria antitoxin was instituted. Convalescence was uneventful. Four successive cultures of material from the nose and throat were submitted during a period of six weeks and all were negative for Corynebacterium diphtheriae. The authors conclude that despite the infrequency of the occurrence of diphtheria organisms among nonimmunized patients who have chronic nasal infections, material from the nose should be cultured for diphtheria organisms. Carriers who have been cured should be checked periodically.

Annals of Surgery, Philadelphia

127:577-768 (April) 1948. **Partial Index**

Marrow-Nailing of Recent Fractures, Pseudarthrosis and Bone Plastic: Experiences in 100 Cases. A. Westerborn.—p. 577.
Cardiac Resuscitation. R. D. Dripps, C. K. Kirby, Julian Johnson and W. H. Erb.—p. 592.
*Metabolic Study of Burn Cases. J. W. Keyser.—p. 605.
Surgical Triangles of Inguinopectineal Region (Inguina): Their Classification, Parietal Relationship and Significance in Hernia Repair. F. E. Dugdale and C. C. Burton.—p. 627.
*Thyroiditis. G. Crile Jr.—p. 640.
Coarctation and Aneurysm of Aorta: Report of Case Treated by Excision and End-to-End Suture of Aorta. H. B. Shumacker Jr.—p. 655.
Uterine Anomaly: Duplication of Uterus, Three Tubes and Three Ovaries: Report of Case. W. N. Rowley.—p. 676.
Selection of Patients for Thoracolumbar Sympathectomy: Description of Set of Rules for Elimination of Failures and Fatalities. J. W. Hinton and J. W. Lord Jr.—p. 681.
"Functional" Subclavian Arterial Murmur: Possible Relation to Scalenus Anticus Syndrome, Costoclavicular Compression, or Neurovascular Syndrome of Wright. R. B. Pomerantz.—p. 688.
Peripheral Nerve Surgery: Repair of Nerve Defects. E. G. Grantham and C. Pollard Jr.—p. 696.
Myxoma, Tumor of Primitive Mesenchyme. A. P. Stout.—p. 706.
Raynaud's Phenomenon and Atypical Causalgia: Role of Sympathectomy. L. J. Kleinsasser.—p. 720.
Multiple Intussusceptions, Direct and Retrograde, of Traumatic Origin. W. H. Falor.—p. 730.
Carcinosarcoma of Uterus. J. R. Lisa, H. Hartmann, I. Bayer.—p. 738.
Congenital Absence of Gallbladder with Case Report. L. Villareal.—p. 745.
Lipoma of Duodenum Causing Melena. T. D. Allison and J. R. Babcock.—p. 754.
New Method of Restoring Continuity of Alimentary Canal in Cases of Congenital Atresia of Esophagus with Trachea-Esophageal Fistula Not Treated by Immediate Primary Anastomosis. R. H. Sweet.—p. 757.

Metabolic Study in Cases of Burns.—Keyser studied the daily urinary nitrogen excretion in 20 cases of burns. Only a few showed an average daily nitrogen excretion considerably greater than normal and in many patients it was somewhat low. Nitrogen balances were determined sixteen times in 7 cases. In 5 of these the nitrogen in the exudate from the burned area was measured. The tendency for the nitrogen balance in burned patients to become negative was confirmed, but negative balances seemed to be due to low intake rather than to increased loss of nitrogen. Exudate nitrogen, measured in 10 cases, made up from 2 to 25 per cent of the total nitrogen output (excluding feces). A fall in plasma protein was observed soon after burning in 3 cases in which serial determinations were made over several days. Low plasma protein values were encountered in other cases also. Creatinuria was observed in 3 men with burns of 7 per cent, 15 per cent and 20 per cent of the body surface. Proteinuria was observed in many cases, especially in those with the more extensive burns. Plasma chloride was determined at intervals in a number of cases and correlated with urine chloride. The fall in plasma chloride noted by some earlier investigators was confirmed and is discussed in relation to intravenous plasma therapy. Blood sugar levels (venous blood, Folin-Wu method) after burns of various degrees of severity were measured in 11 cases. In 2 cases hyperglycemia was certain, and in a few others values were perhaps slightly high.

Thyroiditis.—Crile reports on three types of thyroiditis: 27 instances of subacute thyroiditis; 14 of struma lymphomatosa, and 11 of Riedel's struma. The facts that subacute thyroiditis is almost always associated with pain and tenderness and that these symptoms only rarely occur in the other types are evidence against the possibility that subacute thyroiditis represents an early stage of the more chronic processes. The facts that Riedel's struma is more often unilateral, that struma

lymphomatosa usually involves the entire thyroid and that adenomas are frequently present in Riedel's struma but rarely if ever recognized in struma lymphomatosa are further evidence against progress of one lesion to the other. It is possible that subacute thyroiditis is the result of a virus infection. Struma lymphomatosa appears to be a systemic disease, possibly of the deficiency type. Further study of its relationship to achlorhydria, anemia, generalized lymphoid hyperplasia and possibly to vitamin or other deficiencies is indicated. Riedel's thyroiditis appears to be a proliferative form of fibrosis usually centering about a degenerating adenoma. Roentgen irradiation is the treatment of choice for subacute thyroiditis. Thiouracil may be of value. In the rare cases of struma lymphomatosa in which the diagnosis is made before operation roentgen irradiation should be given a trial. If struma lymphomatosa is recognized at the time of operation a conservative resection of both lobes of the thyroid is recommended. The morbidity of radical resection is high. In Riedel's struma roentgen rays are of little value. If the onion-like concentric laminations in the fibrous tissue surrounding the central degenerating adenoma can be found, these avascular planes can be followed by blunt dissection and the core of the lobe shelled out without disturbing its capsule. Symptoms are relieved after this procedure.

Archives of Pathology, Chicago

45:135-270 (Feb.) 1948

Morphologic Study of Cardiac Conduction System: V. Pathogenesis of Heart Block and Bundle Branch Block. D. J. Glomset and R. F. Birge.—p. 135.
Manifold Manifestations of Reticulo-Endothelial Disease: Report of Case of Hodgkin's Disease (Lymphogranulomatosis), Acute Hemolytic Anemia and Giant Follicular Lymphadenopathy. C. G. Tedeschi and T. J. Carnicelli.—p. 171.
Spread of Carcinoma to Spleen: Its Relation to Generalized Carcinomatous Spread. J. W. Harman and P. Dacorso.—p. 179.
*Laennec Cirrhosis: Its Histogenesis, with Special Reference to Role of Angiogenesis. E. Moschcowitz.—p. 187.
Statistical and Histologic Study of One Hundred and Twenty Canine Neoplasms. R. M. Mulligan.—p. 216.
Mastitis of Mouse as Related to Postsecretory Mammary Involution. W. L. Williams and R. A. Patnode.—p. 229.
Role Played by Salivary Glands in "Alarm Reaction." W. E. Ehrich and J. Seifter.—p. 239.
Normal Variation of Costochondral Junction. J. Cohen.—p. 246.

Laennec Cirrhosis.—In order to study the histogenesis from the biologic as opposed to the static point of view, Moschcowitz examined lesions from the earliest to the most mature phase in serial sections. His studies were made on 75 livers in all stages of cirrhosis. There was evidence that the earliest stage of Laennec cirrhosis is invariably a fatty liver. Transformation of fatty liver to cirrhosis may be caused by interaction of nutritional deficiency and a deficiency of lipotropic factors. If a proper diet is instituted, the fat eventually becomes more or less depleted, but this does not necessarily prevent the cirrhotic process from continuing, at least for a certain period. Under favorable conditions, the cirrhotic process may cease, and the end result is "latent cirrhosis." The first evidence of beginning cirrhosis is an inflammatory reaction, with round cells, monocytes, plasma cells and a few polymorphonuclear leukocytes infiltrating the periportal spaces. This is the exudative phase. The succeeding phase is a productive one and is represented by a fibroblastic transformation. The third phase is the formation of a capillary network in these areas. The further development of these capillaries proceeds according to the laws of Thoma. Many of the capillaries collapse, and the resulting cells evolute into progressive fibrosis and ultimately sclerosis. Other capillaries maintain their integrity and, according to the laws of Thoma, lengthen and enlarge and serve as the main blood supply of the granulomatous and fibrous strands. Serial section shows that these vessels communicate with the portal veins. No evidence is found of an arterial supply of these strands. This further evolution is similar to that in the embryo and in granulation tissue. These granulomatous areas at first penetrate into the interlobular septal spaces or into the lobule and unite with similar adjacent projections from other portal spaces. Often they unite with projections from the hepatic veins, partially converting the blood supply of the liver as in an Eck fistula. These have been termed bivenous strands. This distribution forms the typical pattern in Laennec cirrhosis. The progressive sclerosis and its elastic transformation convert the liver from a hypertrophic to an atrophic one. In this interpretation the connective tissue structure is the result of the multipotential properties of the cells of the adult mesenchyma, which maintain in a large measure their embryonic potentialities.

Archives of Surgery, Chicago

56:125-258 (Feb.) 1948

*Principal Indications for Splenectomy During Childhood. G. Van Buren and G. M. Curtis.—p. 125.
Plastic Surgical Repair of Facial Paralysis. P. W. Greeley.—p. 132.
Tonus of Bladder During Spinal "Shock." R. M. Nesbit and J. Lapides.—p. 138.
Total Gastrectomy with Esophagoduodenal Anastomosis. J. T. Priestley and F. Kumpuris.—p. 145.
*Ligation of Splenic Artery in Patients with Portal Hypertension. T. C. Everson and W. H. Cole.—p. 153.
Aeroembolism of Bone Marrow: Experimental Study. P. C. Colonna and E. D. Jones.—p. 161.
Treatment of Carcinoma of t Fundus Uteri. L. S. McGoogan and H. B. Hunt.—p. 172.
Unusual Proliferative Reactions to Suture Material. J. A. Witter. p. 178.
*Phlebothrombosis Associated with Mucin-Producing Carcinomas of Tail and Body of Pancreas: Clinicopathologic Study of 2 Cases with Necropsy. W. K. Jennings and W. O. Russell.—p. 186.
Surgical Treatment of Carcinoma of Ampulla of Vater and Extrahepatic Bile Ducts. V. E. Siler and M. M. Zinninger.—p. 199.
Bilateral Cervical Ribs Associated with Neuropathic Joints. A. F. Jonas Jr., and W. S. Rise.—p. 224.
Femoral Hernia: Treatment and Results. R. F. Mueller.—p. 229.
Congenital Diaphragmatic Hernia: Anatomic and Surgical Importance of Left Triangular Ligament of Liver. P. Thorek.—p. 238.
Absorption of Blood from Peritoneal Cavity. C. R. Snead.—p. 249.

Splenectomy During Childhood.—Splenectomy was performed on 55 children at the Surgical Department of Ohio State University College between 1933 and 1946. Van Buren and Curtis cite following indications for the operation: congenital hemolytic icterus, thrombopenic purpura and the Banti syndrome. Splenectomy was also performed for splenic panhematocytopenia, traumatic rupture, sickle cell anemia, hypoplastic anemia, Gaucher's disease and pseudohemophilia. The age of the infant with congenital hemolytic icterus should be no contraindication to splenectomy. The youngest patient in this group was 30 days old. There was 1 fatality in 20 children subjected to splenectomy on account of congenital hemolytic icterus. As to the indications in thrombopenic purpura, the authors feel that splenectomy is not contraindicated even in the presence of an acute crisis, provided adequate preoperative blood transfusions are given. Delay in removing the spleen may result in a fatality. Two of the 22 patients with thrombopenic purpura were treated with preliminary supportive measures, but despite medical management the condition of the children became progressively worse. Emergency splenectomy in both instances proved efficacious. The remaining 20 were operated on during the interval of quiescence. There was 1 fatality after splenectomy. In the 7 patients in whom the condition was diagnosed as Banti's syndrome, the changes observed in the spleen after splenectomy were compatible with those commonly found. One of the 7 patients with Banti's syndrome died after splenectomy. Accessory spleens were found in 2 of the 22 children with thrombopenic purpura and in 13 of the 20 children with congenital hemolytic icterus. Failure to remove the accessory spleen at the time of splenectomy may result in a recurrence.

Ligation of Splenic Artery in Portal Hypertension.—According to Everson and Cole the portacaval shunt type of operation appears to offer the greatest promise for the relief of the distressing effects of portal hypertension. It is, however, an operation of considerable magnitude, and places a tremendous additional load on an already overtaxed patient. The procedure which they emphasize for poor risk patients is ligation of the splenic artery. This operation is a relatively minor intervention when compared with splenectomy or portacaval shunt. The procedure is not new, but it has not been widely used. After ligation of the splenic artery 1 of the 3 patients operated on showed immediate improvement, which has persisted up to date (one year after operation). The second patient is alive almost three years since the operation. Ascites has not improved appreciably, but the patient reports subjective improvement. This, together with the length of the survival period, suggests that the ligation of the splenic artery was of some benefit. The third patient died four months after the

ligation. Experience with omentopexy performed in their cases and the work of Cates indicate that the favorable results are not due to this procedure. Ligation of the splenic artery will not replace portacaval shunt in the treatment of portal hypertension. It is indicated in patients who could not tolerate the more extensive procedure. Even though there is an appreciable decrease in the size of the spleen after ligation, there was no evidence of necrosis.

Phlebothrombosis Associated with Carcinomas of Pancreas.—Jennings and Russell add 2 cases to the list of malignant pancreatic tumors associated with a thrombotic tendency. The pathologic study of the two patients demonstrated remarkably similar pathologic changes. In each there was a carcinoma of the tail or the body of the pancreas in which the tumor cells were producing intracellular and extracellular substance. One of the tumors was producing an abundant amount of basophilic-staining mucus, while in the other only a small amount of intracellular and extracellular substance was demonstrated. There was associated phlebothrombosis involving both the portal and the systemic venous systems in each case. The most reasonable explanation for the phlebothrombosis was some alteration of the blood-clotting mechanism. These 2 cases are examples of a characteristic syndrome, in which a high incidence of phlebothrombosis is associated with carcinomas arising in the tail or the body of the pancreas. Specific knowledge concerning the relationship of disturbance in the mechanism of blood coagulation to the syndrome under consideration might prove helpful in the establishment of an early diagnosis. To date, no clearcut clinical differentiation has been made between multiple thrombophlebitis ("migrating phlebitis") and multiple phlebothrombosis. Once these two conditions can be established as separate clinical entities, it is possible that a definite clue may be had to the existence of mucinous carcinoma situated in the pancreas, stomach or lung, the odds greatly favoring the first-mentioned organ. Such evidence may well constitute an indication for abdominal exploration and possible cure of the disease.

Endocrinology, Springfield, Ill.

42:153-236 (March) 1948. **Partial Index**

Effect of Dietary Protein Content On Nitrogen Retention and Weight Gain Produced by Hypophyseal Growth Hormone. G. S. Gordan, L. L. Bennett, C. H. Li and H. M. Evans.—p. 153.
Attempt to Explain Anomalous Action of Lugol's Solution in Exophthalmic Goiter. J. F. McClendon, W. C. Foster and J. W. Cavett.—p. 168.
Metabolism of Steroid Hormones: Isolation of Etiocholanediol-3(Alpha), 17(Alpha) from Human Urine. A. M. Miller and R. I. Dorfman.—p. 174.
Pathology of Adrenal Gland in Addison's Disease with Special Reference to Adrenocortical Contraction. N. B. Friedman.—p. 181.
Progesterone and Desoxycorticosterone in Steroid Control of Gonadotrophic Function of Hypophysis: Exemplified by Behavior of Intrasplenic Ovarian Graft in Guinea Pig. A. Lipschutz, R. Iglesias, S. Bruzzone, J. Humerez and J. M. Penaranda.—p. 201.
Effect of Dietary Protein Concentration On Secretion of Adrenocorticotrophin. F. Moya, J. L. Prado, R. Rodriguez, and others.—p. 223.

Illinois Medical Journal, Chicago

93:3-64 (April) 1948

*Surgical Treatment of Psychoses. E. Liebert and L. Davis.—p. 203.
*Influence of Insulin on Degenerative Changes in Diabetes Mellitus. R. N. Hedges.—p. 206.
Maternal Death Study: Pleas for Instituting an Illinois State-Wide Program. C. Newberger and R. R. Cross.—p. 210.
Osteomyelitis of Face and Skull. H. Brunner.—p. 213.
Hydatiform Mole with Eclampsia Occurring in Fourth Month of Pregnancy. B. J. Winston.—p. 221.

Surgical Treatment of Psychoses.—Liebert and Davis review the results obtained with prefrontal lobotomy in 38 cases. Twenty-five patients improved and of the improved patients 12 were discharged from the institution. Thirteen patients remained unimproved. All of the patients subjected to prefrontal lobotomy had been ill for many years and constituted a severe behavior problem in a mental institution. Untoward effects of the operation as incontinence of urine, epileptic seizures and lack of initiative following the operation, must be expected in some cases.

Insulin and the Degenerative Changes in Diabetes Mellitus.—Hedges points out that more attention must be given to such early degenerative changes in diabetes mellitus as albuminuria, moderate hypertension and beginning retinitis, rather than to the development of arteriosclerosis in the extremities, if one is to prolong the life of diabetic persons and protect them against complications. At present little is done except attempting to control the blood sugar through the use of diet and insulin, and, while insulin may control glycemia, it does not check the development of degenerative lesions. More information is required on the need for additional insulin in diabetic patients when infection is present and more attention must be given to the acceleration of degenerative processes in diabetic patients, for at present there is no treatment for these.

Journal of Clin. Endocrinology, Springfield, Ill.

8:3-209-268 (March) 1948

Studies in Serum Electrolytes. XVI. Changes in Serum and Body Fluids in Anorexia Nervosa. F. W. Sunderman and E. Rose.—p. 209.
Diurnal Rhythm in Excretion of Neutral Reducing Lipids by Man and Its Relation to 17-Ketosteroid Rhythm. G. Pincus, Louise P. Romanoff and J. Carlo.—p. 221.
Effects of Starvation on Sex Hormones in Male. E. C. Jacobs.—p. 227.
Rapid Rat Test for Pregnancy: Ovarian Hyperemia Response as Routine Diagnostic Procedure. G. M. Riley, Marjorie H. Smith and Pearl Brown.—p. 233.
Adrenal Cortical Hormone Excretion in Endocrine and Nonendocrine Disease as Measured by Chemical Assay. W. H. Daughaday, H. Jaffe and R. H. Williams.—p. 244.
Relation of Obesity to Function of Thyroid Gland, Especially as Indicated by Protein-Bound Iodine Concentration in Plasma. R. H. Williams.—p. 257.
Studies on Antihormone Specificity with Particular Reference to Gonadotropic Therapy in Female. J. H. Leathem and A. E. Rakoff.—p. 262.

Journal of Investigative Dermatology, Baltimore

10:227-300 (April) 1948. **Partial Index**

Specificity of Streptococci Isolated from Patients with Skin Diseases: Studies on Pemphigus, Dermatitis Herpetiformis, Lupus Erythematosus and Erythema Multiforme: II. Dermatitis Herpetiformis. A. L. Welsh.—p. 231.
Studies on Effect of PH and Solubility on Antifungal Properties of Fatty Acids, Trimethyl Cetyl Ammonium Pentachlorphenate and Other Agents. E. J. Foley and S. W. Lee.—p. 249.
Method for Study of Penetrability of Liquid and Semisolid Films Used in Skin Protection. H. Eisner.—p. 273.
Provocative Test for Assaying the Dermatitis Hazards of Dyes and Finishes Used on Nylon. A. J. Fleming.—p. 281.
Field Trial of United States Army Fungicidal Ointment. M. Sullivan and H. A. Fishbein.—p. 293.

Journal of Nervous and Mental Disease, New York

107:313-410 (April) 1948

Motility, Behavior and the Brain: Stereodynamic Organization and Neural Co-Ordinates of Behavior. P. I. Yakovlev.—p. 313.
Alterations of Behavior Produced in Cats by Lesions in the Brainstem. P. Bailey.—p. 336.
Basic Pathology of Schizophrenia. J. M. Nielsen.—p. 340.
Studies in Electronarcosis Therapy: II. Physiologic Effects in Electronarcosis and Electro Shock. A. Simon, K. M. Bowman and Nellie Halliday.—p. 358.
Studies in Electronarcosis Therapy: III. Psychologic Test Findings. R. E. Harris, K. M. Bowman and A. Simon.—p. 371.
Electric Shock Therapy in General Paresis. H. C. Solomon, A. S. Rose and R. E. Arnot.—p. 377.
Significance of Phenomenon of Extinction. S. B. Wortis, M. B. Bender and H. L. Teuber.—p. 382.
Cerebral Localization of Psychologic Processes Occurring During a Two-Minute Experience. S. D. Ingham.—p. 388.

Journal of Pediatrics, St. Louis

32:333-478 (April) 1948

Hunger Edema in Children. E. P. Petrides.—p. 333.
*Sublingual Methyl Testosterone for Boyhood Emotional, Physical, and Genital Immaturity. F. E. Harding.—p. 351.
Cerebral Complications in Pertussis. A. M. Litvak, H. Gibel, S. E. Rosenthal and P. Rosenblatt.—p. 357.
Pediatric Deaths in Large General Hospital. R. V. Platou, J. Kometani and N. C. Woody.—p. 380.
*Nontuberculous Pulmonary Calcification. A. D. Biggs and R. G. Rigby.—p. 393.
Receding Chin and Glossoptosis. A Cause of Respiratory Difficulty in Infant. A. Nisenson.—p. 397.

Sublingual Methyl Testosterone for Immaturity in Boys.—Harding says that in boys with unusually small genitalia a neurosis may be caused by the fear of abnormality. Methyl testosterone enlarges all parts of the male genitalia before or during puberty. When small doses of it are given, it does not initiate the onset of puberty in a child too young for the occurrence. Methyl testosterone was administered in small daily doses to a selected group of 58 boys between the ages of 7 and 15 years. Tablets of methyl testosterone were held under the tongue or between the teeth and the cheek and were allowed

to dissolve slowly. They each contained 5.0 mg. of material and were cut in half or in fourths for the 2.5 mg. or 1.2 mg. doses. The total daily dose varied between 0.6 and 10 mg. Treatment was continued for two to twenty months. Genital development was considered satisfactory in all patients taking methyl testosterone. Satisfactory development of primary and secondary sex characteristics occurred. In some patients there was an increase in weight and production of greater muscular strength. The average rate of growth as determined by height was increased to 3.2 inches (8.1 cm.) per year. The neuroses due to the presence of unusually small genitalia were cured. There was less emotional immaturity.

Nontuberculous Pulmonary Calcification.—Biggs and Rigby point out that calcium deposits in the lungs or at their hili were always considered to be pathognomonic of tuberculosis. In recent years evidence has accumulated that there are other causes of pulmonary calcification. The authors obtained consistently negative tuberculin reactions in 14 children who had calcium deposits in the chest. One child had Boeck's sarcoid involving the lungs without cough. Acid-fast bacilli were demonstrated by direct smear in the secretion aspirated through the bronchoscope in this 1 patient only. The authors regard bronchoscopic methods of study in questionable cases of tuberculosis as valuable. A thorough clinical study, including bronchoscopy and bacteriologic study of the aspirated secretions, failed to produce evidence that these children had or had had a tuberculous infection. Eight of these 13 patients with pulmonary calcification had some change in the mucous membrane at the bifurcation or in the main bronchi. Eight had a history of frequent colds or persistent coughs. Twelve of the 13 were given cutaneous tests with histoplasmin. Six of the 12 gave an immediate reaction to histoplasmin. On the basis of these observations and of reports in the literature the authors conclude that pulmonary calcification may be caused by factors other than pulmonary tuberculosis. It has not been definitely determined what these factors are, but there is suggestive evidence that a mild subclinical histoplasmosis may be one of them. Ordinary recurrent infections of the respiratory tract may be another.

Journal Pharmacology & Exper. Therap., Baltimore

92:363-466 (April) 1948. **Partial Index**

Pharmacology of Compounds Structurally Related to Hydroxytyramine. A. M. Lands, V. L. Nash, B. L. Dertinger and others.—p. 369.
*Efficacy of BAL (2,3-Dimercaptopropanol) in Treatment of Experimental Lead Poisoning in Rabbits. F. G. Germuth Jr., and H. Eagle. —p. 397.
Histamine Shock in Mice Sensitized with Hemophilus Pertussis Vaccine. I. A. Parfentjev and Mary A. Goodline.—p. 411.
Acute Vascular Tolerance to Morphine, Isonipecaine (Demerol), and Methadon (Amidone) in Dog. F. E. Shideman and H. T. Johnson. —p. 414.
Inhibition of Pancreatic Vacuolization. A. L. Tucker.—p. 421.
Improved Colorimetric Method for Estimation of Histamine. S. M. Rosenthal and H. Tabor.—p. 425.
Response of Isolated Hypodynamic Myocardium to Inotropic Drugs. L. J. Sciarini, Elizabeth M. Ackerman and W. T. Salter.—p. 432.
Isodynamic Equivalents of Digitoxin Congeners as Tested on Hypodynamic Myocardium. W. F. White, J. Belford and W. T. Salter. —p. 443.
Action of P-Aminosalicylic Acid (PAS) in Experimental Tuberculosis. W. T McClosky, M. I. Smith and J. E. G. Frias.—p. 447.
Curariform Activity of d-N-Methyl-isochondrodendrine and d-O-Methyl-isochondrodendrine. D. F. Marsh and M. H. Pelletier.—p. 454.

BAL in Experimental Lead Poisoning.—The experiments described by Germuth and Eagle proved that BAL (2,3-dimercaptopropanol) failed to protect rabbits that had been poisoned with lead acetate. At times it actually accelerated the toxic effects of lead acetate in rabbits. The experimental lead poisoning produced in rabbits by either the subcutaneous or the intravenous injection of lead acetate differs so materially from that seen in man, with respect to the route of administration, the chemical form of the lead, the chronicity of the intoxication and the organs affected, that the results obtained with BAL in these experimental animals have no necessary significance with respect to its possible therapeutic activity in man. Despite the present complete failure of BAL to detoxify lead in rabbits, its effect on the urinary excretion of lead was so striking as perhaps to justify its cautious therapeutic trial in human cases. For two hours after a single injection of BAL at 20 mg. per kilogram of weight, the urinary excretion of lead increased eleven to forty fold in animals with a subcutaneous depot, and three to seven fold in animals injected intravenously. This favorable effect on the excretion of lead lasted for approximately four hours after a single injection of BAL.

Kentucky Medical Journal, Bowling Green

46:73-112 (March) 1948

Management of Fractures Below the Knee. J. P. Glenn.—p. 77.
Blood Dyscrasias in Adults: Hypersplenism. M. F. Beard.—p. 84.
Psycho Surgery. R. J. Angelucci.—p. 89.
Endemic Typhus Fever. J. T. Gilbert Jr.—p. 94.
Typhus Survey in Bowling Green, Kentucky. P. H. Harden.—p. 98.
Prophylaxis as Well as Therapeusis in Toxemia of Pregnancy. G. G. Greene.—p. 100.
Twenty-Three Cases of Pulmonary Tuberculosis Treated with Streptomycin. R. Starr.—p. 105.

Medical Annals of District of Columbia, Washington

17:191-256 (April) 1948

Medical Preparedness in Atomic Defense. C. J. Brown.—p. 191.
Therapy of the Aged. E. J. Stieglitz.—p. 197.
Gastrointestinal Endoscopy. I. B. Brick.—p. 205.
Surgical Treatment of Hypertension. W. S. McCune.—p. 210.
Surgical Treatment of Carcinoma of Head of the Pancreas and of Thyroid: Report of a Case. P. C. Kiernan.—p. 216.
*Use of Penicillin in Weil's Disease: Report of 2 Cases. J. M. Moser Jr.—p. 219.

Penicillin in Weil's Disease.—Moser reports 2 men, aged 30 and 27, respectively, with symptoms of Weil's disease and a history of probable contact with rats while swimming and camping. Treatment with sulfadiazine had failed; penicillin in doses of 50,000 units every two hours was given for 12 doses, and after that at somewhat longer intervals. These cases suggest that penicillin is effective if given during the bacteremic phase. There is no way of making the diagnosis except by finding the leptospirae in blood smears during the first week. This is difficult for the ordinary laboratory technician. If the physician withholds the therapy until after the diagnosis has been made, the effectiveness of penicillin becomes progressively diminished and the disease may be fatal. The reason that penicillin loses its effectiveness after the onset of jaundice or nephritis is perhaps that the spirochetes take up residence in all the organs of the body and high therapeutic concentrations of penicillin cannot reach them. The author bases his belief that penicillin produced the clinical cure in the 2 cases on the definite improvement in the temperature curve within twenty-four hours after the beginning of penicillin therapy; the moderate Herxheimer reactions which the patients demonstrated after their second injection of penicillin, and the general clinical improvement. The failure of complete clinical recovery in the first case as manifested by fatigability and headaches suggests the existence of low grade hepatitis, which took six months of good diet to clear up.

Michigan State Medical Society Journal, Lansing

47:363-456 (April) 1948

Cytologic Study of Bronchial Secretions in Diagnosis of Bronchogenic Carcinoma: Short Review. H. M. Smathers.—p. 393.
Primary Carcinoma of Lung: Report of 100 Cases. N. Levitt.—p. 395.
Diagnosis and Treatment of Breast Tumors. F. A. Coller.—p. 399.
Tuberculous Child: Reflections on Problems of Prophylaxis and Recent Advances in Therapy. R. V. Platou.—p. 400.
*Mercurial Diuretics in Paroxysmal Nocturnal Dyspnea. R. A. Sokolov. —p. 404.
Proctologic Principles in Hemorrhoidectomy. J. F. Wenzel.—p. 408.
Potentialities and Limitations of Prenatal Pediatrics. C. A. Smith. —p. 411.

Mercurial Diuretics in Paroxysmal Nocturnal Dyspnea.—Sokolov presents observations on 47 patients with evidence of left ventricular failure and, more particularly, paroxysmal nocturnal dyspnea. The treatment of the individual attack of paroxysmal dyspnea was along conventional lines. Morphine in ¼ to ½ grain (16 to 32 mg.) doses was given hypodermically, usually in conjunction with 1/100 grain (0.6 mg.) of atropine. When indicated, oxygen via tent was also supplied. If the patient had not been previously digitalized, rapid digitalization was induced by giving 1.2 mg. of digitoxin in twelve hours, to be followed by a daily maintenance dose of 0.1 to 0.2 mg. Bed rest was enforced for a varying length of time. If the patient was overweight, a low caloric diet was prescribed. Regardless of the patient's weight, a salt-poor regimen was instituted.

Many of these patients ultimately required more energetic diuresis, so that mercurial diuresis was made an integral part of the treatment in all cases in which no contraindication existed. Acidifying agents, such as ammonium chloride, enhance the diuretic effect of the mercurials. The mercurial diuretic used was meralluride. The first dose of meralluride is 1 cc. intravenously. This is followed in four days by a 2 cc. dose. Thereafter injections of 2 cc. are given once a week until the patient is considered stabilized. At this point the interval between injections is lengthened as much as possible. Mercurials should not be given in the presence of severe renal disease, in severely dehydrated patients or those with depleted serum chlorides, in the moribund, in the presence of shock associated with recent myocardial infarction, in patients having previously exhibited idiosyncrasy to the drug and in the presence of large amounts of digitalis-containing edema fluid. The author emphasizes that, although this treatment is not new, its value has been inadequately emphasized.

New England Journal of Medicine, Boston

238:583-614 (April 22) 1948

*Carcinoma of Stomach. C. E. Welch and A. W. Allen.—p. 583.
Complete Heart Block. Study of Two Cases in Veterans of World War II. C. Fisch.—p. 589.
Vaccination Against Influenza A and B. Comparison of Reactions, Doses and Titer Responses of Two Different Vaccines in Infants and Children. R. I. Lienke, P. Crump and J. M. Adams.—p. 593.
Acute Meningitis Caused by Neisseria Sicca. Charlotte Bansmer and J. Brem.—p. 596.
Cancer. G. W. Taylor.—p. 598.
Mucous Carcinoma of Stomach, Signet Ring Type.—p. 602.
Adenocarcinoma of Ascending Colon, with Metastases to Liver. Thrombophlebitis of Both Femoral and Iliac Veins and of Inferior Vena Cava.—p. 604.

Carcinoma of Stomach.—Welch and Allen review observations on patients with carcinoma of the stomach admitted to the Massachusetts General Hospital during the ten year period 1937 to 1946. Comparison with earlier reports shows that the delay before treatment has remained unchanged, averaging five months. A more aggressive attitude toward gastric ulcer has increased the recognition of early cancer of the stomach. The introduction of a transthoracic approach and the wider use of total abdominal gastrectomy have increased the number of cases available for resection. The mortality for gastric resections for cancer has dropped to a present level of 17 per cent for the entire series and to 11 per cent in the last five year period. The mortality for subtotal resections in which all gross disease is removed has been 3 per cent in the last five year period. Meanwhile, the number of patients not operated on has declined, so that 75 per cent have an operation. Fifty per cent of the total have a gastrectomy, either subtotal or total. The best palliative operation, if gross disease cannot be removed, is subtotal gastrectomy. The five year survival rate is now 7 per cent of the entire group that enters the hospital. The most fruitful method now available to increase the number of cures of cancer of the stomach is to reduce the delay from onset of symptoms to surgical intervention.

Public Health Reports, Washington, D.C.

63:501-528 (April 16) 1948

Program of National Cancer Institute. W. Carrigan and Ora Marshino.—p. 501.

63:529-556 (April 23) 1948

Employment of Soluble Antigen in Screening Tests for Typhus Complement Fixation. T. O. Berge.—p. 529.
Statistical Studies of Heart Diseases, Part I. Heart Diseases and Allied Causes of Death in Relation to Age Changes in the Population. I. M. Moriyama and Mary Gover.—p. 537.

63:557-592 (April 30) 1948

Operation of United States Public Health Service Malaria Control Program. F. Tetzlaff.—p. 557.
*Dental Effects of Community Waters Accidentally Fluorinated for Nineteen Years: II. Differences in Extent of Caries Reduction among Different Types of Permanent Teeth. H. Klein.—p. 563.
Diphtheria Epidemic in Utah in 1947. A. A. Jenkins.—p. 573.
Appearance of "Minimus" Type Diphtheria in Utah. T. W. Galbraith, R. S. Fraser and E. H. Bramhall.—p. 577.

Dental Effects of Fluorinated Waters.—The study reported by Klein is based on examination of nearly 2,000 children residing in New Jersey and more than 6,000 children of Hagerstown, Md. Of the New Jersey children ranging in age from 5 to 19 years, 874 were born and reared in a fluoride area, 725 moved into the fluoride area at various ages subsequent to birth in places outside the fluoride areas and 340 children were lifetime residents of the nonfluoride area. The depressant effect of fluorides on caries may be approximately of equal potential for all the different types of teeth. Because of the different gradients in the characteristic or expected caries susceptibilities of the different teeth, the resultant effect may be a variation in the per cent reduction of caries among the different teeth. Consideration of the differences in caries reduction among the different teeth leads to the view that the differential effects are perhaps related to basic differences in the characteristic susceptibilities of the different teeth. Even after prenatal exposure and a postnatal residence of fifteen to nineteen years in a fluoride environment, caries attack is reduced only by about a third of normal expectation in the lower molar teeth of lifetime residents. Although this is a significant reduction, particularly from the point of view of the total need for dental service in the population, it is necessary to recognize that approximately two thirds of the treatment problem for caries still arises among molars in the fluoride area.

Rhode Island Medical Journal, Providence

31:153-220 (March) 1948

The Position of General Practitioner Today. J. M. Faulkner.—p. 167.
Leaves Off The Tree. R. Fitz.—p. 171.
Graduate Medical Education and Hospital Economics. O. G. Pratt.—p. 177.
Admission to Medical Schools. D. O'Hara.—p. 186.
Intern Training in Hospital System. C. F. Wilkinson Jr.—p. 201.

31:227-276 (April) 1948

Conquest of Puerperal Infection 1846-1946. E. S. Brackett.—p. 235.
Tuberculosis in Providence. P. F. Harrington.—p. 240.
Symposium on Rheumatic Fever and Heart Disease. E. F. Kelly, Banice Feinberg, F. V. Corrigan and J. F. Kenney.—p. 243.
Responsibility of Hospital Administrator to Other Community Health Agencies. I. V. Hiscock.—p. 250.

Surgery, Gynecology and Obstetrics, Chicago

86:513-640 (May) 1948

Aortic Valvulotomy: Experimental Methods and Early Results. H. G. Smithy, H. R. Pratt-Thomas and H. P. Deyerle.—p. 513.
*Studies on Vagotomy in Treatment of Peptic Ulcer: II. Clinical Evaluation. K. A. Meyer, P. A. Rosi and I. F. Stein Jr.—p. 524.
Steel Wire Sutures, Local Anesthesia, and Immediate Ambulation in Treatment of Hernia. G. H. Pratt.—p. 530.
Studies on Spinal Cord Injuries: III. Altered Reflex Activity. J. Martin and L. Davis.—p. 535.
Atypical Adynamic Ileus Apparently Caused by Nutritional (Thiamin Chloride) Deficiency: Report of 6 Cases. D. J. Leithauser.—p. 543.
Observations on Use of Gelatin Sponge in Closure of Experimentally Produced Defects of Bronchus. C. R. Hanlon.—p. 551.
*Discrepancies in Myelography: Statistical Survey of 200 Operative Cases Undergoing Pantopaque Myelography. W. B. Scoville, W. H. Moretz and W. D. Hankins.—p. 559.
Wound Healing in Early Ambulation. H. P. Royster, Lillian I. McCain and A. Sloan.—p. 565.
Differential Spinal Block: IV. Investigation of Intestinal Dyskinesia, Colonic Atony and Visceral Afferent Fibers. S. J. Sarnoff, Julia G. Arrowood and W. P. Chapman.—p. 571.
Biologic Chemistry of Wound Healing: I. Effect of dl-Methionine on Healing of Wounds in Protein-Depleted Animals. S. A. Localio, Margaret E. Morgan and J. W. Hinton.—p. 582.
Tumors of Testicle. H. R. Sauer, E. M. Watson and E. M. Burke.—p. 591.
*Correction of Hypoproteinemia by Administration of Plasma and Blood. J. G. Allen, G. Bogardus, W. Egner and D. B. Phemister.—p. 604.
Electrocardiogram in Biliary Tract Disease and During Experimental Biliary Distention: Clinical Observations on 26 Patients. G. B. Hodge and A. L. Messer.—p. 617.

Vagotomy in Peptic Ulcer.—Meyer and his associates report 35 cases in which previous medical or surgical management had failed to give relief from ulcer pain. There were 16 instances of previous perforation. Nineteen patients had had previous bleeding. Repeated attacks of severe epigastric pain were present in 31 of the 35 patients, and in 12 the pain was intractable. Duodenal ulcer was present in 26 patients, marginal ulcer in 7 patients; 1 patient had a gastrojejunal colic fistula and 1 had a prepyloric ulcer. The transthoracic approach was employed in the first 9 cases and the transabdominal approach in the remaining 26. The latter is now preferred, because of several advantages. All patients had immediate relief from ulcer pain. Thirty-one of the 35 are leading an

unrestricted life for the first time in many years. Dietary and medical treatment has been completely eliminated. The majority of patients noted a change in the bowel habit. They had one or two soft bowel movements a day, whereas preoperatively almost every patient gave a history of constipation. Thirty-one patients expressed themselves as being well satisfied with the results. One patient died because of uremia and nephrosis which followed a blood transfusion. Recurrence of ulcer symptoms with positive roentgen evidence of peptic ulcer occurred in 4 cases. The symptoms of cardiospasm were noted in 3 patients, but were spontaneously relieved. The most frequent and disturbing complication was gastric retention and distention, but this has been controlled. The permanency of the altered gastric function following a complete vagotomy is not yet certain, and little is known of the effect of vagotomy on the other organs innervated by the vagi. The use of vagotomy should be limited until more information is available. Complete vagotomy is the method of choice in marginal ulcer following gastric resection.

Discrepancies in Myelography.—Scoville and his associates had gained the impression that myelography yields equivocal findings in at least 25 per cent of the cases. This is at variance with published statistics. They analyze 200 consecutive cases in which patients were subjected to pantopaque myelography and operation for a lumbar ruptured intervertebral disk at the Cushing General Hospital. Four cases of lumbar spinal tumors were excluded from the statistics. Ruptured disks were found in 173 of the remaining 196 patients operated on. Findings in the 23 other cases were swollen nerve roots, adhesions, bony ridges, one fractured facet and, more commonly, nothing. Double disks were found in 11 per cent. Over-all errors occurred in 65 out of 196 cases. In order to rule out the personal equation from these diagnostic errors, the authors made a comparison with two surveys made by other investigators. Clinical evidence of a ruptured disk is more important than is myelographic evidence. A positive myelogram is more important than a negative one. A normal myelogram in the face of clinical evidence of a ruptured disk will be wrong three out of four times. Myelography fails to rule out the presence of a laterally placed lumbosacral disk. When myelography is used as the sole diagnostic criterion, the over-all error is in the neighborhood of 25 to 35 per cent in contrast to the 6 to 8 per cent cited in the literature. The authors will continue to use myelography routinely on all persons suspected of having ruptured disks, but will tend to discount all normal myelograms if contradicted by the clinical findings.

Correction of Hypoproteinemia by Plasma and Blood.—Allen and his associates report a study of 9 hypoproteinemic patients who were given large volumes of plasma in an endeavor to elevate the plasma proteins. Whole blood was sometimes given to correct anemia, but in all but 2 patients the greatest source of parenteral protein was plasma. The amounts of plasma, usually given daily, were large as measured by current practice, but the amount of nitrogen given by this method was less than that advocated when protein hydrolysates are used for this purpose. The increase in the plasma protein concentration was rapid after these quantities of plasma and blood were given. Normal values were usually established within five to seven days. Nitrogen balance studies and plasma volume changes in 6 of these patients showed that most of the transfused plasma probably left the blood stream within a day or two. That which could not be accounted for on the basis of an increase of total circulating plasma protein may possibly have been recast as tissue protein, since there was little, if any, evidence of a latent increased nitrogen excretion. Larger amounts of plasma and blood were required to elevate the plasma protein concentration in the more severely starved patient than in the better nourished one, even though the plasma protein concentrations were reduced to similar levels in both groups. This work suggests that the fear of overtransfusion is unwarranted except when the cardiovascular reserve is reduced. It emphasizes the wisdom of using blood in some patients in place of plasma because of the gain in oxygen-carrying cells and the possible utilization of hemoglobin to form tissue proteins.

Union Médicale du Canada, Montreal

77:517-652 (May) 1948. **Partial Index**

Prevention of Whooping Cough by Vaccination. L. Forté and A. Frappier.—p. 528.
*Commentary on Tuberculosis of Larynx. J. Brahy.—p. 537.
Spontaneous Abortion and Its Treatment with Progesterone. A. Cousineau.—p. 543.
Biliary Peritonitis. R. Grignon.—p. 547.
Medical Applications of Genetics. M. Moreno.—p. 551.
Physical Therapy and Occupational Therapy in Psychiatry. J. Faure.—p. 554.
Simple Skin Grafts. G. E. Cloutier.—p. 556.

Tuberculosis of Larynx.—According to Brahy, tuberculosis of the larynx is to be considered as a complication of pulmonary tuberculosis exclusively, because primary tuberculous lesions of the larynx have not been demonstrated and tuberculosis of the larynx has not been reported in association with tuberculosis of bones, peritoneum, meninges or eyes. For several years the incidence of advanced cases of pulmonary tuberculosis decreased as the result of a successful campaign against this disease. It also explains the reduced number of cases with laryngeal lesions, which, however, may be observed in two thirds of those cases of pulmonary tuberculosis which cannot be controlled. The age groups between 25 and 40 years are affected most frequently. Laryngeal lesions are observed three times more often in men than in women. One hundred patients with pulmonary tuberculosis, many of whom presented laryngeal lesions, were treated with streptomycin at the hospital of the Sacré-Coeur in Cartierville, Montreal. Five milligrams of the drug was administered by intramuscular route every morning and evening for three weeks. In 1 male patient aged 40 with bilateral pulmonary cavities and considerable involvement of the larynx, the odynophagia subsided completely after the second week of this treatment, and his body weight was increased 25 pounds (11.3 Kg.) after three weeks of treatment. The left half of the larynx was practically healed, while diffuse edema of the right half was still present. The cavity of the right lung did not appear cleared on roentgenologic examination, while the aspect of the left lung was satisfactory. Although not all the other patients were improved to the same degree, it is believed that streptomycin has a favorable effect on the ulcerations of the larynx, leaving a uniform and smooth mucosa. This effect is more pronounced with extensive than with small lesions. The present tendency is to continue the treatment with streptomycin for a period of one hundred and twenty days.

Virginia Medical Monthly, Richmond

75:159-212 (April) 1948

Miscellaneous Observations on Management of Allergic Patient. E. L. Alexander.—p. 161.
Medical Public Relations. J. T. T. Hundley.—p. 167.
Management of Diabetic Coma. J. H. Smith.—p. 171.
Blood Disturbances and Anuria Resulting from Severe Burns. P. J. DeVries and H. Allen.—p. 173.
Medical Care and Hospital Administration. P. S. Smith.—p. 179.
Indications for Broncho-Esophagology. H. D. Hoskins.—p. 182.
Clinical Review of Papillary Adenocarcinoma of Ovary. G. Speck.—p. 185.
Anemia Problem in Everyday Practice. H. C. Brownley.—p. 191.
Cancer Following Burn Scars. H. Cantor.—p. 197.
Evaluation of Annual Serologic Test Performance Studies Conducted by Virginia State Health Department from 1940 through 1946. E. M. Holmes Jr.—p. 200.

75:213-262 (May) 1948

Medical Legislation in 1948 Virginia General Assembly. R. C. Duval Jr.—p. 213.
Contributions of 1948 General Assembly in Field of Health. L. J. Roper.—p. 217.
Management of Early Syphilis. D. C. Smith and R. C. Thompson.—p. 219.
Q Fever: Case Report. T. J. McGurl, J. P. Williams.—p. 225.
Treatment of Phlebitis and Its Complications. A. Bigger.—p. 229.
Report of Infestation of Intestinal Parasites Throughout Virginia. Lula W. Garst and A. W. Bengtson.—p. 231.
Vocational Rehabilitation a Resource for Physicians. R. M. Hoover.—p. 233.
Hemoglobin Studies on Albemarle County School Children. T. S. Englar, Ruth Blakely and W. Wilkins.—p. 236.
Microscopic Examination of Exfoliated Cells as an Aid in Early Cancer Diagnosis. G. Cooper Jr.—p. 241.
Management of Peripheral Vascular Disease. N. Bloom.—p. 248.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

British Journal of Ophthalmology, London

32:193-256 (April) 1948. **Partial Index**

Clinical Report on Miners' Nystagmus. Dorothy A. Campbell.—p. 193.
Dark Adaptation of Coal Miners Suffering from Nystagmus. F. W. Sharpley.—p. 199.
Psychiatric Aspect of Miners' Nystagmus. I. E. S. Stern.—p. 209.
Binocular Vision in Miners. Dorothy A. Campbell, Renee Harrison and Jean Vertigen.—p. 226.

British Medical Journal, London

1:627-672 (April 3) 1948

Public Health Laboratory Service. G. S. Wilson.—p. 627.
Identification of Medical Documents. L. Hogben, M. M. Johnstone and K. W. Cross.—p. 632.
Treatment of Hyperidrosis. H. A. Haxton.—p. 636.
Immediate Prostatectomy for Retention of Urine. G. A. Bagot.—p. 638.
Some Simple Observations on Transfusion Reactions. J. Wallace and R. D. Richards.—p. 640.
Iso-Immunization by Blood Factor N. L. De Kromme and L. A. M. Van Der Spek.—p. 643.

1:673-718 (April 10) 1948

Surgical Teaching in America. A. E. Porritt.—p. 673.
Public Health Laboratory Service: Origin and Development of Public Health Laboratories. G. S. Wilson.—p. 677.
Guterman Test in Threatened Abortion: Report Based on 100 Consecutive Cases. S. Bender.—p. 683.
Guterman Test for Pregnancy. W. H. H. Merivale.—p. 685.
Hydrolysis of Protein in Cartilage and Bone. P. Pincus.—p. 687.
Yearly Re-Examination of Factory Group by Mass Miniature Radiography. W. Pointon Dick.—p. 689.

Edinburgh Medical Journal

55:129-192 (March) 1948

Short History of Pneumococcus with Special Reference to Lobar Pneumonia. J. T. Smeall.—p. 129.
Preparation of Iso-Osmotic Phosphate Buffer Solutions. E. B. Hendry. —p. 142.
Mortality from Appendicitis in Scotland 1901-45. J. B. De W. Molony. —p. 153.
Symposium on Headache as a Symptom: I. General Considerations. W. A. Alexander.—p. 168.
Id.: II. Migraine. J. K. Slater.—p. 173.
Id.: III. Psychologic Aspect. W. M. C. Harrowes.—p. 176.
Id.: IV. The Eyes and Headache. H. M. Traquair.—p. 180.
Id.: V. Headache from Sinus Infections. A. B. Smith.—p. 183.

Lancet, London

1:505-544 (April 3) 1948

*Measured Radical Gastrectomy: Review of 505 Operations for Peptic Ulcer. A. H. Visick.—p. 505.
Penicillin and Sulfonamides in Typhoid Fever: Experience of Physicians in Military Hospitals in Middle East. C. G. Parsons.—p. 510.
Physiologic Jaundice of Newborn. Some New Measurements of Factors Concerned. P. L. Mollison.—p. 513.
Combined Chaulmoograte and Sulphone Treatment of Leprosy and Tuberculosis. L. Rogers.—p. 515.
Normal Temperatures in Old Age. T. H. Howell.—p. 517.
Treatment of Angina of Effort with Androgens. V. K. Summers. —p. 519.

1:545-580 (April 10) 1948

*Penicillin and Sulfathiazole in Typhoid Fever. Clinical Trial. G. Bevan, Marjorie V. N. Sudds, R. Evans and others.—p. 545.
Weight Changes in Pregnancy. J. A. Scott and B. Benjamin.—p. 550.
*Measured Radical Gastrectomy. A. H. Visick.—p. 551.
Sterile Splenic Abscess After Relapsing Fever. L. A. Nasr.—p. 555.
Reducing Substances in Urine in Pregnancy and Early Puerperium. H. E. Archer and B. J. Haram.—p. 558.
Primary Atypical Pneumonia: Small Highly Infective Outbreak. B. G. Alton and M. D. Hickey.—p. 559.

Penicillin and Sulfathiazole in Typhoid.—Bevan and associates point out that considerable interest was aroused when Bigger in 1946 found that typhoid bacilli are effectively inhibited in the test tube by the combined action of penicillin and sulfathiazole. A typhoid outbreak in which the vehicle of infection was ice cream infected by a urinary carrier offered an opportunity for a trial of the combined penicillin-sulfathiazole treatment. The 39 patients who received courses of combined penicillin and sulfathiazole, similar to those found effective by McSweeney in 1946, did not show the speedy disappearance of toxemia and subsidence of pyrexia described by McSweeney. Three small groups of patients treated with penicillin-sulfathiazole were compared with three untreated control groups. There was no evidence of an appreciable clinical effect of the drug treatment. There were no fatalities in the largest group of 25 treated patients, but 5 of the patients whose condition caused the greatest anxiety had been given Felix's "Vi + O" antityphoid serum. A considerable proportion of patients yielded positive blood cultures shortly after completion of their courses of penicillin-sulfathiazole treatment. Fecal excretion of typhoid bacilli during convalescence was not shorter in the treated groups than in the controls. The typhoid strain responsible for the reported outbreak was not more resistant to the action of penicillin and sulfathiazole than were four other strains with which it was compared in tests in vitro. The authors warn against the indiscriminate use of penicillin and sulfathiazole in the treatment of typhoid.

Measured Radical Gastrectomy.—In this review of 505 operations for peptic ulcer Visick asserts that the essential point of technic of a measured radical gastrectomy is division of all but one of the vasa brevia and all branches of the left gastro-epiploic artery. This makes it possible to leave a small devascularized gastric remnant 1½ inches (3.8 cm.) and 3 inches (7.6 cm.) long on the lesser and greater curvatures, respectively. A measured radical gastrectomy differs from a conventional three-quarters resection in three respects: (1) the area of stomach which remains can be measured and controlled with accuracy; (2) the gastric remnant is extensively devascularized, and (3) in 98 per cent of cases permanent relative achlorhydria is produced. The operative mortality for the last 430 gastrectomies was 3.7 per cent. A penetrating ulcer caused twice the operative mortality of a nonpenetrating ulcer. If the history was over five years, the operative mortality was increased two and one-half times. One patient among 155 under the age of 40 died. The operative mortality among patients aged 40 to 49 was 5 per cent; aged 50 to 59, it was 5.8 per cent, and 60 and over, 7.1 per cent. Of the 430 patients examined from six months to twelve years after operation 95.1 per cent showed satisfactory results. The year by year continuous follow-up indicates that results improve with time. The proportion of patients who are free of symptoms at six months (47 per cent) rises to 63 per cent at forty-two months after operation. Women were more liable to have minor symptoms resulting from operation. In spite of wide resection macrocytic anemia has not been discovered. No ulcer recurred later than eighteen months after gastrectomy.

Medical Journal of Australia, Sydney

1:321-356 (March 13) 1948

The Individual and the Environment. A. A. Abbie.—p. 321.
Hypothalamus and Obesity. C. Brooks.—p. 327.
Inguinal Hernia: Review of Treatment. G. Brosnan.—p. 331.
Tuberculosis of Upper Part of Respiratory Tract, with a Report of Case. D. B. Rosenthal.—p. 335.
*Four Cases of Carditis Occurring in Children and Associated with Administration of a Foreign Serum. Joan Storey.—p. 337.

Carditis Following Administration of Foreign Serum.—According to Storey there is a close analogy between certain of the symptoms of rheumatic fever and those of serum sickness. Polyarthritis, fever, rashes and lymph node enlargement may occur in both. In view of the present theory that rheumatic fever may be akin to an allergic reaction, a hypersensitivity to the hemolytic streptococcus group A, the author pursued the analogy of the 2 cases more closely. The greatest danger in rheumatic fever is in the damage done to the heart, and this is not ordinarily a feature of serum sickness. The 4 cases cited by the author have in common the development of polyarthritis, fever, raised blood sedimentation rate and carditis following the injection of a foreign serum. In the last 3 cases serum sickness occurred in the interval between the injection of the serum and the discovery of carditis. It is well within the bounds of possibility that these children suffered an attack of rheumatic fever in which the "Phase 1" infection passed unnoticed and that the serum sickness, which developed more quickly than usual after injection of serum, was purely coincidental. This is especially so in view of the fact that the administration of tetanus antiserum is a fairly common procedure and that these 4 cases were selected from over a thousand histories of rheumatic fever investigated. A second explanation

is that given by Wadsworth and Brown, who, in discussing their case of carditis, pointed out that there is much to favor the assumption that carditis may have been reactivation of subclinical rheumatic fever by protein shock.

1:357-388 (March 20) 1948

Anne MacKenzie Oration. F. S. Hone.—p. 357.
Protein Deficiency and Use of Human Serum in Its Treatment. J. Isbister.—p. 362.

1:389-420 (March 27) 1948

*Pneumonokoniosis in New South Wales Coal Miners. A. T. Nisbet.—p. 389.
Occlusive Arterial Disease. E. Downie.—p. 396.
Alcaptonuria with Report of an Additional Case. A. Basser.—p. 400.
Method for Equilibration of Blood with Gas Mixture. Alice J. Palmer and M. J. Morrissey.—p. 401.

Pneumonoconiosis In Coal Miners.—Nisbet describes how the "Special Pneumonokoniosis Board of New South Wales" operates, and attempts to evaluate the cause of fibrosis of the lung tissue on the basis of nearly fifteen years' experience as radiologist to this special board. It is unfortunate that the two different terms "reticulosis" and "nodular fibrosis" are used by separate authorities to mean the same thing, anthracosis. Silica is the cause of the disability in coal miners as well as in other miners. Miners working in a pit with the greater content of silica in the coal or seam, and therefore in the dust, will show the greater percentage of cases of pulmonary disease. The quartz miner may contract silicosis in five to seven years; the metal worker without proper precautions in under ten years; the asbestos worker, the flour miller and others take longer still. The soft coal miner must work at least twenty years before manifestations of anthracosis occur. The incidence among coal miners in New South Wales of superadded tuberculosis appears far less than that among the remainder of the population. The total incidence of men with incapacitating pulmonary fibrosis due to dust was 4.90 per thousand colliery employees per year.

Proceedings of Royal Society of Medicine, London

41:187-260 (April) 1948. Partial Index

*Serious Limitations and Erroneous Indications of Biopsy in Diagnosis of Tumors of Bone. J. F. Brailsford.—p. 225.
Surgery in Treatment of Rheumatoid Arthritis and Ankylosing Spondylitis. W. A. Law.—p. 251.

Limitations of Biopsy in Bone Tumor.—Brailsford shows that it is erroneous to suppose that biopsy will permit the surgeon to establish whether a bone tumor is benign or malignant, when clinical and roentgenographic observations by competent observers have failed to clarify this question. Actually biopsy may add conflicting evidence which will delay the accurate diagnosis. Ultimate resolution of a bone tumor which had clinical, roentgenographic and even histologic appearances of malignancy is the best evidence of simplicity. In view of the not uncommon occurrence of such cases, it is unjustifiable to record lesions as "fully proved" malignant tumors if amputation results in cure. A malignant bone tumor appears to indicate a local expression of a constitutional disturbance, which may disappear when the patient is given the essential corrective; for in spite of the earliest amputation similar lesions may develop at any time after, even with twenty years' symptomless interval. Yet primary lesions and the multiple associated lesions which have the features of metastases may resolve completely or sufficiently to permit of the average duration of symptomless normal life. The response of carcinomatous metastases from some primary carcinomas in the breast or prostate to diethylstilbestrol gives hope that some such hormone will be found to cure sarcoma. In the investigation of bone tumor particular attention must be paid to hereditary dysplasia or dystrophy, the possibility of vitamin deficiency, endocrine or blood disorder, infection or trauma. If the roentgenographic appearances indicate a simple lesion the appropriate treatment should be given. If the lesion has the roentgenographic features which suggest malignancy the only treatment which present imperfect knowledge dictates is amputation. This is an irrevocable procedure, the success of which cannot be predetermined. As the roentgenographic appearances can be closely mimicked by inflammatory or deficiency and other disorders, it would be reasonable in any doubtful case to give a course of appropriate medication, and if this fails, a course of high voltage roentgen therapy. Even when it is established beyond doubt that the tumor is malignant and amputation is decided on, there appears to be some justification in preceding this with a full sarcoma dose of roentgen rays.

Thorax, London

3:1-52 (March) 1948

Hydatid Disease of Lung. A. Logan and H. Nicholson.—p. 1.
Dissociated Paralysis of Diaphragm Following Phrenic Crush and Pneumoperitoneum. W. Fox.—p. 15.
*Peptic Ulcer of Esophagus. P. R. Allison.—p. 20.
Calcified Foci Within Thorax of English Children. B. C. Thompson.—p. 43.
Intra-Pulmonary Calcification and Histoplasmin Sensitivity. B. H. McCracken.—p. 45.
Cavernous Hemangioma of Lung: Report of Case. W. P. Cleland.—p. 48.

Peptic Ulcer of Esophagus.—Allison shows that for a long time peptic ulceration of the lower part of the esophagus did not receive proper attention, but more accurate observation in recent years has led to more frequent diagnosis of these ulcers. Seventy-four instances of this condition have been studied in the thoracic surgical unit at the General Infirmary at Leeds. Dysphagia always more marked for solid foods than for liquids, was the symptom that brought most of these patients to the hospital. Dyspepsia was present in about three fourths of the patients. It occurred in 1 of 3 forms: (1) high epigastric discomfort associated with high acid secretion and related to disturbances of gastric motility; (2) burning pain behind the sternum caused by acid bathing the lower end of the inflamed esophagus, and (3) a more boring type of pain passing into the back between the shoulder blades and often made worse by flexion of the spine. Diaphragmatic defect is the most important etiologic factor. Heterotopic gastric mucosa in the esophagus accounts for few. Congenitally short esophagus occurs but rarely; it has not been seen in this series. Defects in the diaphragm allow herniation of the cardia into the mediastinum and so render ineffective the mechanism for keeping acid out of the esophagus. These hernias may be congenital (congenital short esophagus), infantile or acquired. There are 7 examples in infants in the present series. The acquired group includes 4 patients in whom ulceration followed gastroesophageal anastomosis after excision of carcinoma of the cardia.

Tubercle, London

29:73-96 (April) 1948

*Significance of Tuberculin Sensitivity. I. Bluhm.—p. 73.
Mass X-ray and Health Propaganda. Jocelyn Goldsbrough.—p. 82.
BCG Vaccination of Nurses. J. Heimbeck.—p. 84.

Significance of Tuberculin Sensitivity.—In order to find out whether there exists a connection between the size of the tuberculin reaction and the tuberculous infection, Bluhm studied a series of healthy persons and of persons with tuberculosis. The investigation has been carried out at the Central Dispensary of Stockholm. He employed dosages of 0.05 mg. of old tuberculin. The sensitivity has been evaluated by measuring the length and breadth of the red papule. In persons without manifest tuberculosis, who live in a milieu in which tubercle bacilli are to be found, tuberculin sensitivity is usually increased. If the source of infection is removed, the reaction decreases. The cause of hypersensitivity is probably a continuous exposure to tubercle bacilli. Thus if persons without tuberculosis prove hypersensitive, the environment should be investigated. In persons with manifest tuberculosis there is a certain regularity in the fluctuation of the tuberculin reaction. In persons with erythema nodosum and primary pulmonary tuberculosis tuberculin sensitivity is usually much increased. Sensitivity seems to be maximum in an early phase of the infection. Tuberculin sensitivity shows a gradual decrease on repeated testing. In patients with exudative pleurisy the reaction is comparatively low. In pulmonary tuberculosis sensitivity is stronger in the exudative than in the productive cases. In healed tuberculosis exposure to tuberculosis may bring about an increase in the reaction even though no fresh lesions appear. In pulmonary tuberculosis with cavities, in which the lesions are productive or exudative-productive, sensitivity is also low. It seems that the variation in sensitivity does not depend so much on whether the disease is extensive, progressive or regressive as on whether it is in an exudative or a productive phase.

Acta Medica Scandinavica, Stockholm

130:1-106 (March 10) 1948. **Partial Index**

Investigations on Acute Infections of the Respiratory Tract: IV. Experimental Studies on Effect of Small Doses of Sulfonamides in Respiratory Tract Infections. G. Löfström.—p. 1.

Clinical Problems Concerning Fatty Liver and Methylation Processes. P. Astrup.—p. 12.

Myocardial Infarction Resulting from Intravenous Administration of Hypertonic Solution of Sodium Chloride to Patients with Arteriosclerosis Obliterans of Lower Extremities.—p. 26.

*Porphyrin in Urine as First Symptom of Lead Poisoning. C. D. de Langen and J. A. G. ten Berg.—p. 37.

Resorption of Penicillin After Inhalation. P. Dragsted and M. Schwartz. —p. 45.

Porphyrin in Urine as First Symptom of Lead Poisoning.—De Langen and ten Berg found that increased excretion of porphyrin in the urine was an early sign of lead poisoning among the population of a district in which the water contained comparatively large quantities of lead. The semiquantitative method found useful in these investigations requires 20 cc. of urine, to which are added some drops of glacial acetic acid and 2 cc. of ether. The test tube is shaken and is examined under ultraviolet light, in which the layer of ether fluoresces. In the presence of a normal porphyrin content of the urine the fluorescence is light blue to green, but in the presence of increased porphyrin content gradually deepening red fluorescence appears as the porphyrin content increases. In case of an equivocal result a quantitative method can be employed. This method is also described. The aforementioned method appeared to be more reliable for detecting the first signs of lead poisoning than the basophile granulation of the erythrocytes. This was proved (1) by a comparative examination of both criteria in 87 persons who all had more or less high excretion of porphyrin due to intake of lead and (2) by an experimental examination of normal persons taking predetermined quantities of lead. The authors are convinced that in the routine control of workers in the industries using lead the semiquantitative porphyrin method is much better than looking for basophile granulation.

Acta Radiologica, Stockholm

29:189-278 (March 31) 1948. **Partial Index**

*Influence of Castration by Roentgen Rays on Carcinoma of Breast. V. E. Thayssen.—p. 189.

*Protrusion of Acetabulums as Complication of Labor. J. Petersen. —p. 205.

Roentgen Diagnosis of Fluid in Frontal and Sphenoidal Sinuses. D. Turesson.—p. 215.

Microcolon: With Report of Two Cases. J. Zimmer.—p. 228.

Roentgen Examination in Acute Dilatation of Stomach. J. F. Dahl. —p. 237.

Treatment of Keloids at Radiumhemmet 1921-1941. F. Jacobsson. —p. 251.

Influence of Roentgen Castration in Carcinoma of Breast.—Thayssen states that at the Radium Center in Copenhagen several hundred patients were treated between 1934 and 1943 for cancer of the breast with metastases. Of these, 99 were given local treatment of both the primary tumor and the metastases, and underwent roentgen castration some time after the appearance of the metastases, whereas the others got only local roentgen treatment. It was found that 40 per cent of the castrated patients were still living two years after the appearance of the metastases as against only 11 per cent of 100 controls. Of 74 patients given roentgen treatment before or after operation and castrated, 28 per cent were alive five years after the operation, as against 8 per cent of the controls. On the basis of 79 urinalyses for gonadotropin and estrogen it is shown that the castration may have a highly beneficent effect even in cases in which the estrogen output was low also before the castration.

Protrusion of Acetabulums in Labor.—Petersen says that although it had been suggested many years ago that protrusion of the acetabulum could be the cause of dystocia, no case seems to have been reported until one was observed at the author's hospital in 1944. The patient was a primipara, aged 32, in whom delivery was protracted (about forty-five hours) and in whom both the clinical and the roentgenologic examinations, as well as the pressure traces on the skull of the child, make it probable that the protraction was due to protrusion of the patient's acetabulums. The chief feature of protrusion of the acetabulum or Otto's disease is an abnormally strong dome-shaped projection of the floor of the acetabulum into the small pelvis. The author discusses the cause of the disease.

Analecta Medica, Mexico, D.F.

8:1-54 (July-Sept.) 1947. **Partial Index**

*Isoimmunization of Mother for Factor of "A" Blood Group of Fetus. R. Medina Aguilar.—p. 49.

Isoimmunization of Mother from Fetus of A Blood Group.—The subject of this report, a woman 37 years of age, had had 9 normal children and 3 abortions. Her blood was of group B, Rh positive and MN positive. There was no syphilis in the family. In the course of the thirteenth pregnancy she contracted moderate diabetes and moderate hypochromic anemia. Her blood serum agglutinated blood of the A group, both Rh positive and Rh negative. It did not agglutinate blood of either B or O groups. After inactivation it hemolyzed blood serum of the A blood group. The father's blood was of group A, Rh positive and also MN positive. The children belong to A, AB or O blood groups. All are Rh positive. The patient was brought to the hospital with acute hemorrhage from placenta previa with a dead fetus whose blood was of group A, Rh positive and MN positive. The fetus presented hepatomegaly, splenomegaly and blood containing 84 per cent erythroblasts, the majority of which were of the Lendorff type. The liver and the spleen contained large numbers of erythroblastic nests which greatly damaged the structure of the organs. The findings in the fetus clarified the isoimmunization of the mother of the B blood group by a fetus of the A blood group, notwithstanding the fact that both the mother's and the fetus's blood were Rh positive and also MN positive.

Annales Pædiatrici, Basel

170:113-168 (March) 1948. **Partial Index**

*Banti's Complex of Symptoms and Its Relations to Occult Malaria During Childhood. A. Eckstein.—p. 113.

Tropical Aspects of Pathology of Liver in Pediatrics. E. Stransky and F. Dauis Lawas.—p. 131.

Synechia Vulvae in Children. K. Vesely.—p. 151.

Banti's Disease and Occult Malaria During Childhood.—Eckstein of Ankara believes that in the presence of disorders that show splenomegaly, degeneration of splenic tissue and its replacement by connective tissue, Banti's syndrome will have to be considered, if malaria, kala-azar, cirrhosis, glycogen disease, Niemann-Pick's disease and the like can be ruled out. Further advancement in diagnostic procedures will probably limit the concept of Banti's disease more and more and replace its diagnosis by one of the aforementioned group. The author cites a case in which repeated examinations of the blood and of the sternal and splenic punctates and observation of the temperature justified the diagnosis of Banti's disease after all other possibilities, particularly malaria and kala-azar, had been ruled out. When the spleen, which weighed 3½ Kg. (7 pounds, 11 ounces), was removed it showed histologically only degeneration with proliferation of the connective tissue, while the characteristic signs of malaria (plasmodia and pigment) were absent. Immediately after the operation the typical picture of tertian malaria (type of temperature curve, tertian ring forms) developed. There existed in this case an occult form of malaria which had presented the picture of "Banti's disease." In spite of the splenectomy there were no complications, and the patient was eventually cured after several relapses. The case corroborates earlier impressions that malaria in patients without a spleen is not necessarily extremely serious or even fatal as some authors have claimed. The author feels that splenectomy is justified in similar cases.

Arch. Hosp. Clin. Niños Roberto del Rio, Santiago

15:151-208 (Dec.) 1947. **Partial Index**

*Leukemias in Infancy. A. Costa.—p. 158.

Leukemia in Infants and Children.—Costa reports observations on 37 leukemic patients, between the ages of 6 months and 10 years. There were 25 boys and 12 girls. Leukemia was of the acute type in 29 patients, of the chronic myeloid type in 5 and monocytic in 1. The youngest patient in the group with acute leukemia was 6 months old. Acute leukemia appears to be frequent in infants and in young children. It represents 80 per cent of the total number of cases of infantile leukemia. In acute leukemia of infants and children there are remissions

during which the leukemic changes of the blood are lacking. This fact makes the myelogram of great diagnostic importance. The duration of the disease is short, especially in infants and young children. The clinical and hematologic picture of chronic myeloid leukemia in infants and children is similar to that of adults. The cases of monocytic leukemia observed by the author were all of the Naegeli type and of short course.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

92:681-748 (March 6) 1948. **Partial Index**

*Electrocardiogram and Patent Ductus Botalli. W. den Boer.—p. 698.
Phrenic Shoulder Pain. G. J. Smelt.—p. 706.

Electrocardiogram and Open Ductus Botalli.—According to den Boer 3 children with symptoms of patent ductus arteriosus (Botalli) were seen during the last year at the clinic in Utrecht. Deviation in the electrocardiogram of the axis to the left may occur, but a decided deviation to the right makes it almost certain that the open ductus is complicated by other defects such as pulmonary stenosis, or that a patent ductus arteriosus does not exist. Deviation of the axis to the right is a contraindication to operative treatment. The electrocardiographic examination is of great value in the differentiation of patent ductus arteriosus with and without complications. It will help prevent operations where they are not advisable and will also prevent bringing an otherwise valuable operation into discredit.

Nordisk Medicin, Stockholm

37:299-348 (Feb. 13) 1948. **Partial Index**

Chemotherapy in Rheumatic Polyarthritis. N. Svartz.—p. 299.
*Gold Treatment in Chronic Polyarthritis. F. Sundelin.—p. 303.
*Chronic Polyarthritis in Children and Gold Treatment. B. S. V. Bille. —p. 307.
Myasthenia. S. Refsum.—p. 311.

Gold Treatment in Chronic Polyarthritis.—Reactions or complications were seen in 50 per cent of 2,817 courses of treatment in 1,904 cases of polyarthritis treated with gold in the last five years; only 4.5 per cent of the complications were grave and led to the interruption of the treatment. Seven cases were fatal. On completion of treatment fully 90 per cent of the patients were subjectively and objectively improved both as to local symptoms and general condition. Preliminary report on late results shows that of 300 patients given treatment with colloidal gold completed at least three years ago 273 continue fully or partly able to work. Because of its effectiveness, treatment with colloidal gold occupies a special place among the therapeutic means tried to date in chronic polyarthritis. The treatment must be given under close control of the patient. The dosage must be comparatively high to insure quick and adequate results. Large doses do not entail greater risk than small doses. The complications are often associated with rapid improvement in the articular symptoms. The grave complications consist of extensive and prolonged dermatitis, granulocytopenia and thrombopenic purpura; also encephalitis and bronchopneumonia. The author does not repeat the treatment in a patient who has had thrombopenic purpura. Arteriosclerotic patients with hypertension and with cardiac injuries and some patients with nephritis occasionally evince low tolerance to treatment with colloidal gold.

Chronic Polyarthritis in Children and Gold Treatment.—Bille reports on 43 cases of the disease in children under 15 given treatment with colloidal gold; in 46 cases intramuscularly, in 16 intravenously, in 2 by mouth, with one injection a week and usually from six to ten injections in each course, under close control with examination of the blood and urine at least once between injections and daily control of the temperature. In all, sixty-four courses were given. The treatment was individualized, with initial dose usually of 5 to 40 mg. depending on the body weight, highest dose form 20 to 150 mg., the total amount in a course of ten injections from 100 to 1,000 mg. The treatment gave good results in 25 children; 11 were somewhat improved, and 7 unchanged. Complications, almost all mild, appeared in about half the courses of treatment and were independent of the amount of gold given. Encephalitis and purpura are the most dangerous complications in adults. None of the children had encephalitis; 1 case of purpura, with recovery, was the most serious complication in these cases. Albuminuria occurred more often than in adults.

Pediatria del Medico Pratico, Turin

22:271-312 (Oct.) 1947. **Partial Index**

*Congenital Hemolytic Disease: Prevention and Therapy. E. Lattes, p. 271.

Congenital Hemolytic Disease.—Prevention of the disease includes avoiding transfusion or intramuscular injections of Rh-positive blood into infant girls, girls and women all through their life of sexual activity when the blood of the infant, girl or woman is Rh negative. In case of isoimmunization of the mother, the sudden increase or lowering of blood antibodies after the eighth month of pregnancy is an indication for induction of delivery and replacement of the newborn infant's blood by transfusion immediately after birth. Transfusion of this type is also indicated immediately after birth in cases of acute jaundice in infants born at full term to isoimmunized mothers. Blood in the amount of 500 cc. is administered. Transfusion of Rh-negative blood is indicated in the great majority of cases of anemia from congenital hemolytic disease. The author reports good results with blood transfusion in 5 cases.

22:313-340 (Nov.-Dec.) 1947. **Partial Index**

*Penicillin Therapy of Purulent Pleurisy and of Pulmonary Abscess in Infants. F. Toscano.—p. 323.

Penicillin Therapy of Purulent Pleurisy and of Pulmonary Abscess.—Combined intrapleural and intramuscular penicillin therapy is of value in purulent pleurisy of infants. Toscano reports favorable results in 7 cases. Pulmonary abscesses require continued introduction of penicillin into the abscess by means of aerosol inhalations. The solution of penicillin to be nebulized in oxygen should contain from 20,000 to 100,000 Oxford units of penicillin for each cubic centimeter of the solution. The patient should inhale from 5 to 8 liters of the oxygen-penicillin nebulization as the total dose.

Presse Médicale, Paris

56:193-204 (March 20) 1948

*Preventive Vaccination Against Whooping Cough and Diphtheria in Infants and Young Children. G. Ramon, R. Debré, M. Lelong, R. Sohier and R. Richou.—p. 193.
*Modified and Latent Forms of Acute Meningitis and Abscess of Cerebrum in Patients Treated with Penicillin. L. Rouquès, M. David and Jean Pautrat.—p. 194.
Syndrome of Pancoast and Tobias. J. Chenebault.—p. 195.

Vaccination Against Whooping Cough and Diphtheria.—Ramon and his associates have resumed their investigations on immunization against diphtheria and whooping cough which were begun before the war. They had demonstrated on guinea pigs that when diphtheria toxoid was mixed with antipertussis vaccine its efficacy was increased from three to ten times. The authors continued their studies on experimental animals and on young infants with an antipertussis vaccine which is nonvirulent and nontoxic and to which had been added diphtheria toxoid. The latter was concentrated, purified and freed from foreign elements, so as to avoid reactions to peptones and to other substances derived from the culture. Combining the vaccines not only makes it possible to reduce the quantity to be injected, but increases the chances of success. The authors think that it will be possible to immunize infants before they are 8 months old simultaneously against whooping cough and diphtheria. In the course of the second year of life the child, in accordance with French law, will be subjected to vaccination with a mixture of diphtheria and tetanus toxoids to which should be added avirulent whooping cough vaccine. This last formula will have the advantage of reinforcing the previously induced immunity to diphtheria and whooping cough and confer immunity to tetanus.

Modified Forms of Meningitis and Cerebral Abscess in Patients Treated with Penicillin.—Rouquès and his associates point out that acute meningitis and cerebral abscess of patients treated with penicillin often assume modified aspects and may even remain latent. It is not advisable to wait for the appearance of the classical functional signs before considering the existence of these complications. The authors present 2 cases. One concerned acute febrile meningitis manifested only by intense headache without muscular contracture or changes in the reflexes. The other case was one of a large cerebral abscess with osteomyelitis of the frontal bone; the

condition was so dormant that without the existence of papilledema one would have hesitated to affirm the existence of a pathologic process.

56:301-316 (April 24) 1948

Treatment by Transplantation of Tissues According to Filatov's Procedure. P. Wertheimer, R. Gautier and S. Marek.—p. 301.
*"Cure" of So-Called Acute Leukemia. R. Fauvert, J. Mallarmé and P. F. Petit.—p. 302.
*Brucellosis and Rapid Agglutination. J. Basset.—p. 303.

Cure of Acute Leukemia.—According to Fauvert and his co-workers acute leukemia or malignant leukosis is a subacute condition with a prolonged course, spontaneous remissions and occasionally even with a temporarily reversible blood picture. Four cases, in 2 adults and in 2 children, are reported, which presented an initial phase of characteristic and complete leukosis followed by clinical and hematologic remission. The duration of the remission was four years and one year respectively in the adults, and two and one-half months in the children. The treatment of these 4 patients consisted of rest exclusively. These facts must be considered in the evaluation of the efficacy of any therapeutic trial, and results should be acknowledged only after a follow-up of several months. Although satisfactory results had been obtained with penicillin, transfusions or perfusions of citrated blood, they should be considered only as symptomatic treatments. Exsanguination transfusion which was given to children did not prove more effective than simple transfusion or perfusion.

Rapid Agglutination in Brucellosis.—Basset believes that a positive reaction obtained with a rapid antigen may cause an erroneous serum diagnosis of brucellosis when certain unreliable commercial antigens are used. Only antigens should be considered of value which have been standardized and adjusted to the titer of a known serum. The more concentrated or the more rich in microbian bodies an antigen is, the less sensitive it is. For rapid agglutination an antigen of much higher concentration is required than for slow agglutination because of the considerable volume of serum used for rapid agglutination. Procedures are described by which such antigens may be obtained which then may offer considerable aid in the diagnosis of brucellosis at the sick bed.

Revue du Rhumatisme, Paris

15:101-132 (April) 1948. **Partial Index**

*Reducible Discal Hernias: Contribution to Problem of Sciatica Designated as "Nondiscal." S. de Sèze and J. Levernieux.—p. 101.
Lumbar Arthrodesis L-2 L-3 Effected by Anterior Abdominal Approach in Treatment of Post-traumatic Vertebrodiscal Syndrome. S. de Sèze, P. Funk-Brentano and S. H. Jurmand.—p. 106.
Vertebral Accidents in Shock Therapy: Rapid Aggravation After Series of Electro-shocks of Slight Pre-existent Scoliosis. S. de Sèze and J.-C. Dubois.—p. 115.
Latent Spondylolisthesis with Large Spondylolysis of L-5: Roentgenologic Discovery at Time of Acute Volvulus of Stomach. S. de Sèze, J. Durieu and A. Djian.—p. 120.

Reducible Discal Hernias and Sciatica.—Evidence is presented by de Sèze and Levernieux to the effect that certain posterior hernias of the intervertebral disk are reducible. This explains some discrepancies between the clinical aspects and the results of roentgenography. In certain cases, in which clinical signs of discal hernia exist, contrast roentgenography fails to disclose the typical notch. This is not surprising, because the roentgenologic examination is made with the patient in the recumbent posture, usually after rest, and in the posture which gives him the least pain. The discal notch might appear if such a patient were examined, with the aid of morphine, in the position in which the pain is mose severe. The reducibility of some discal hernias explains also a certain number of negative surgical explorations in cases of sciatica which are then referred to as "nondiscal" or not due to herniation of a disk. The surgeon must be able to evaluate the consistency of the disk and must think of the possibility of reducible disk lesions and learn to recognize them. The reducible character of the discal hernia does not necessarily imply the benign character of the painful lumbosciatic syndrome. On the contrary, nothing is more annoying than are these "intermittent" hernias. After much loss of time, an operation may be decided on, but if the hernia is not detected and removed, the operation may be ineffective; if it is recognized exeresis may not suffice. These hernias, which are reducible by rest, pose the question of the advisability of a bone graft.

Revue de la Tuberculose, Paris

12:165-308 (No. 3 & 4) 1948

*Report on Treatment of Tuberculosis With Streptomycin. (Study of 225 Patients). E. Bernard and Miss Alice Lotte in collaboration with B. Kreis, J. S. Bourdin and G. Arnaud.—p. 165.

Streptomycin in Tuberculosis.—Bernard and Lotte treated with streptomycin 225 patients, 78 of whom had tuberculosis of the meninges, 54 miliary tuberculosis, 64 nonmiliary tuberculosis of the lungs, and the remainder tuberculosis of the larynx and pharynx. The average dose administered by intramuscular route was 1.5 Gm. (1,500,000 units) for twenty-four hours. Occasionally the daily dose was increased to 2 Gm., but some patients could tolerate only 1 Gm. or even less. At the initiation of the treatment all the patients were given additional three to eight intraspinal injections of 50,000 to 300,000 units, but in general 100,000 units of streptomycin every second day. The treatment by intramuscular route was continued for several months. There were recurrences in 14 of 22 patients in whom treatment was discontinued spontaneously after two to three months. In 5 patients there were recurrences in the course of the treatment after three to five months and in 1 patient even after seven months of treatment. Untoward reactions consisted of vomiting, vertigo and, in 1 case, erythroderma, but in the majority of the cases these reactions did not recur when the treatment was continued after a temporary discontinuance of three to four days. Vestibular disturbances were observed in 39 per cent of the patients. Thirty-one of the 78 patients with tuberculous meningitis were alive after six to eight months. In 22 of the 54 patients with miliary tuberculosis meningitis supervened before, during or after treatment. Thirty-six of the 54 patients, mostly those without meningitis, survived and presented a complete clearing up of their roentgenograms. Streptomycin proved to be a valuable preoperative or postoperative measure in cases of nonulcerating pulmonary tuberculosis. In laryngeal and pharyngeal tuberculosis the dysphagia subsided and the dysphonia and the lesions improved as result of the treatment with streptomycin. Improvement was obtained in isolated nonstenosing forms of bronchial tuberculosis.

Schweizerische medizinische Wochenscrift, Basel

78:317-344 (April 10) 1948. **Partial Index**

B. C. G. Vaccination: Desirability of Its Introduction in Switzerland. T. Baumann.—p. 317.
Chemotherapy of Tuberculosis. E. Suter.—p. 324.
*Streptomycin in Treatment of Intestinal Tuberculosis. N. Markoff. —p. 329.
*P-Aminosalicylic Acid in Chemotherapy of Tuberculosis. L. Ragaz. —p. 332.

Streptomycin in Intestinal Tuberculosis.—Markoff presents a preliminary report on the supporting effect of streptomycin in the treatment of ulcerative intestinal tuberculosis. Streptomycin is administered parenterally, but also enterally in the form of high enemas with elevation of the pelvis and subsequent placing on the right side. In this way, the streptomycin can be carried to the ileocecal valve and beyond into the distal portions of the small intestine. The region of the ileocecal valve is the most frequent localization of the ulcerous and tumor-like forms of intestinal tuberculosis. The enema is given daily for two weeks. This enteral local treatment of intestinal tuberculosis with streptomycin has proved to be a valuble supportive treatment in the 5 cases in which it was employed. Only six months have elapsed since the authors tried this treatment. Their observations are similar to those in the United States. The intestinal symptoms were greatly improved. Roentgenoscopy suggests a healing of the ulcers, but complete repression of the tuberculous process has not been observed as yet. If the more distal portion of the colon and the rectum are involved, treatment by enema is likewise advisable. If tuberculosis involves the small intestine, particularly the proximal portions, oral therapy with streptomycin could be tried with the same doses as those used for bacillary dysentery.

P-Aminosalicylic Acid in Therapy of Tuberculosis.—Most of the patients treated had a progessive form of tuberculosis and a positive sputum. Internal treatment with divided doses of 10 to 15 Gm. per day, continued for a week and then followed by a week free of treatment, was the method most

commonly employed. This treatment was usually continued for several months. Improvement was observed in from 60 to 70 per cent of the patients with pulmonary tuberculosis. There was improvement in the general condition, increase in weight, decrease in temperature, improvement in the sedimentation rate and decrease in the number of bacilli in the sputum. A patient with renal tuberculosis was free from bacilli after two weeks and free from symptoms after eleven weeks. However, para-aminosalicylic acid did not pass the crucial test; it did not save 4 patients with miliary tuberculosis and 3 with meningitis. Favorable results were obtained in the local treatment of empyemas and abscesses by means of a 10 per cent solution of the drug.

Schweizerische Zeitschrift für Tuberkulose, Basel

5:1-64 (No. 1) 1948. **Partial Index**

Total Atelectasis of Lung with Bronchiectasis as Sequela of Tuberculosis of Hilus Nodes. H. Wissler.—p. 1.
*Bronchoscopic Study and Behavior of Bronchi in Course of Primary and Secondary Stages of Tuberculous Infection. A. Dufourt and P. Mounier-Kuhn.—p. 49.

5:65-126 (No. 2) 1948. **Partial Index**

*Bronchoscopic Study and Behavior of Bronchi in Course of Primary and Secondary Stages of Tuberculous Infection. (Concluded). A. Dufourt and P. Mounier-Kuhn.—p. 65.
Successive Cascation of Both Poles of Primary Tuberculous Complex. Nelly M. Schmid.—p. 100.

Bronchoscopic Study of Primary and Secondary Stages of Tuberculosis.—Dufourt and Mounier-Kuhn report 25 cases of primary infection, tuberculous bacillosis and epituberculosis in 22 female patients between the ages of 2½ and 20 years and in 3 boys between the ages of 12 months and 4 years, on 24 of whom bronchoscopy was carried out. This method of examination has been of considerable aid in elucidating the pulmonary manifestations which follow the primary infection. In uncomplicated primary infections the orifice of the lobar bronchus corresponding to the location of the primary focus appeared usually slightly congested, edematous and covered with a mucous secretion rich in polymorphonuclear leukocytes and macrophagocytes. It may contain bacilli. In cases of chronic epituberculosis edema of the main bronchus of the involved lobe may be the dominating feature, and the narrow central opening may be obstructed by a plug of tightly packed macrophagocytes. Compression of the bronchial wall by enlarged lymph nodes, in addition to the swelling of the mucosa and to the plug of the secreted material, may be responsible for bronchial occlusion. Rupture of a lymph node into a bronchus and formation of fistulas were observed more frequently than it has been presumed. Large fistulas are rare, but small fistulas, either single or multiple, occur frequently; they may be latent or manifested by occasional attacks of cough, pain in the chest or rise of temperature. As a rule the roentgenologic picture of the chest reveals only minimum changes limited to the inferior or median lung fields. The bronchial fistulas may heal completely or they may be responsible for various late clinical syndromes resulting from scar, cicatricial stenosis and bronchogenic dissemination.

Semaine des Hôpitaux de Paris

24:891-912 (April 6) 1948

Pathogenic Study on Origin of Dyspnea Associated With Pneumothorax Causing Suffocation. G. Giraud, A. Balmès and J. Mirouze.—p. 891.
Standardization of Vernes' Test for Serum Diagnosis of Syphilis. R. Bricq, A. Gager and J. Lacapère.—p. 894.
*Recent Observations on Recrudescence of Diphtheria in Europe and on Efficacy of Ramon's Anatoxin. H. and M. Hinglais.—p. 899.

Recrudescence of Diphtheria in Europe.—According to the Hinglaises, diphtheria has become the most common and the most fatal of the epidemic diseases in Europe after World War II. The average number of cases in the Netherlands during the period of 1933 to 1939 was 1,400, as compared to that of 38,000 during the period of 1941 to 1946. The corresponding numbers in Finland were 1,993 and 54,297, respectively; in the Iberian peninsula 1,119 and 27,474 respectively; in France 19,893 during the decade of 1928 to 1938 as compared to 45,541 in 1945; in Belgium 2,090 and 6,099 respectively; in Switzerland 2,264 and 4,981 respectively. In Hungary, where vaccination with Ramon's antitoxin was practiced on a large scale and organized methodically, a definite decrease in the number of cases was observed (from 14,500 in 1934 to 9,576 in 1946), and the same applies to Sweden and Denmark. In England mass vaccination has been carried out since 1940-1941. The average number of cases during the period of 1935 to 1939 was 59,114, with 2,860 deaths (mortality rate 5.8 per cent) as compared with 18,596 in 1945 with 694 deaths and to 12,337 in 1946 with 472 deaths. These data and those published by the health service of New York City demonstrate the decisive part which vaccination played in the regression of the disease in England and in New York City. The rhythm of the drop in the mortality rate was the same as that of the drop in the morbidity rate, which proves that the vaccine is as effective with regard to mild forms as to grave forms of the disease. In spite of a certain failure margin which should not be denied, the methodic application of vaccination in a country may practically eliminate the disease in the course of several years.

24:1011-1034 (April 22) 1948

Isolated Round Tuberculous Focus, Nodular, Pseudotumorous or Pseudocystic on Roentgenologic Examination. (Infiltration of Assmann's Type, Tuberculoma and Definitely Isolated Cavity). R. Kourilsky, M. Fourestier, Miss D. Brille and E. de Saint-Germain.—p. 1011.
*Armstrong's Disease (Lymphocytic Choriomeningitis). B. Kreis.—p. 1018.
Prolonged Icterus in Newborn Due to Incompatibility of Rh Factor. Part Played by Maternal Lactation. G. Desbuquois.—p. 1023.

Lymphocytic Choriomeningitis.—Kreis emphasizes that a filtrable virus which was discovered in the United States, may be the pathogene of certain forms of lymphocytic meningitis in which recovery occurs. History of contact with mice, a prodromal febrile period and a pronounced hyperleukocytosis in the cerebrospinal fluid aid in the diagnosis. The latter may be further confirmed by animal inoculation or by demonstration of certain reactions in the serum. The virus causes a lymphocytic infiltration of the choroid plexus when inoculated into the brain of mice. Experiments in man revealed that the disease may be reproduced experimentally by the subcutaneous, intramuscular or intravenous injection of 2 cc. of an emulsion of brain of mice containing the virus; after an incubation period of thirty-six hours to three days rise in temperature may occur at two or three intervals over a period up to three weeks, and the last febrile attack may be associated with late meningitic symptoms such as headache, vomiting and Kernig's sign. In contrast to the tendency of American authors to consider lymphocytic meningitis and choriomeningitis as synonyms, the virus is responsible for only a small number of these cases. The considerable number of persons examined at random who neutralize the virus suggests that Armstrong's disease is to be considered as one of the most important infections occasioned by an identified serum.

Strasbourg Médical

108:83-94 (March 15) 1948. **Partial Index**

Hemorrhages after Hysterectomy (Fourteen Cases Observed During Two Years). R. Keller and L. Gioanni.—p. 83.
*Calcareous Arteritis and Its Treatment by Parathyroidectomy. A. Jung.—p. 87.

Parathyroidectomy in Calcareous Arteritis.—Jung reports 1 case of chronic hyperparathyroidism in a man aged 53. The patient had generalized arteritis with calcium deposits in the abdominal aorta, in the femoral and posterior tibial arteries, in the internal and external carotid arteries and in the choroid plexus. There was a calcified subacromio-deltoid bursitis and calcium deposits in the epiphysis. There was generalized osteoporosis, paradentosis and multiple dental caries. Abnormally large amounts of calcium were observed in the blood and in the urine. Two parathyroid glands were removed under local anesthesia. The calcemia was reduced from 12.2 mg. per cent to 11 mg. per cent and the calciuria from 40 mg. per cent to 13 mg. per cent. Pain in the back and in the shoulder disappeared and pain in the legs and feet was considerably relieved. Three years after the operation the patient was able to hike in the mountains and had resumed his work as an architect. Previous animal experiments had shown that injections of parathyroid extract in rats produced an increased calcium content of the heart and arteries which can be demonstrated both chemically and histologically. These results suggested the existence of chronic hyperparathyroidism with predominant vascular manifestations. The case reported is to be considered as the first clinical proof.

Book Notices

Pathology of Tumours. By R. A. Willis, D.Sc., M.D., F.R.C.P., Sir William H. Collins Professor of Human and Comparative Pathology, Royal College of Surgeons, London. Cloth. Price, $20. Pp. 1044, with 500 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3; Butterworth & Co., Ltd., 4-5 Bell Yard, Temple Bar, London, W.C. 2, 1948.

The first part, 207 pages, deals with general pathologic aspects of tumors: definition, classification, "innocence and malignancy," experimental production, statistics, tumors in animals, mode of origin, structure and growth, direct spread, metastasis and hypothetic nature of neoplasia. The rest of the text, pages 208 to 992, covers systematically in 50 chapters the tumors in the different parts of the body. This is perhaps the most important, convenient source now available for thorough and reliable information about the pathologic aspects of individual tumors. There is a valuable list of select references at the end of each chapter, frequently with comments. In the case of main references and reviews, the authors' names are in capitals and the full titles are given. The 500 figures are all of personally studied structures, with emphasis on less familiar and special features. Needless repetition is avoided. There are many instructive reports of the author's own observations in Melbourne and London of more or less familiar aspects of tumors. The book is addressed primarily to pathologists, advanced students and investigators, but clinicians with special interest in cancer will find it of great interest and value. Willis states promptly and clearly his own present opinion in disputed matters in order "to avoid noncommittal vagueness," realizing fully that future advances may modify current views. Fourteen years ago Willis published his book on "The Spread of Tumours in the Human Body," also a notable book, and now is "Pathology of Tumours" is welcomed as an outstanding addition, soundly critical and comprehensive, to the literature on tumors.

Annual Review of Physiology. Volume X. Victor E. Hall, Editor, Jefferson M. Crismon and Arthur C. Giese, Associate Editors. Cloth. Price, $6. Pp. 552. Annual Reviews, Inc., and American Physiological Society, Stanford, California, 1948.

The tenth "Annual Review of Physiology" is, like the previous volumes, replete with a wealth of information that has laboratory and clinical value. Practically all the reviews have been obtained from this country; only a few from abroad. Nevertheless, the contained information will interest everyone with research and progressive clinical interest. Included in the contents are discussions of physical properties of protoplasm, physiologic aspects of genetics, developmental physiology, physiology of reproduction, conduction and synaptic transmission in the nervous system, somatic functions of the central nervous system, vision, digestive system, blood cytology, heart, peripheral circulation, metabolic aspects of shock, respiration, anoxia in aviation, regulation of energy exchange, metabolic functions of the endocrine glands, heat and cold, physiology of sweating, pharmacology, the coagulation of blood, hemostasis, physiologic psychology and physiologic effects of radiant energy. This volume will need no introduction to those who are familiar with the earlier reviews. Others who have yet to make their acquaintance with it will find a collection of information that warrants the reputation gained by the book.

Aids to Diagnosis and Treatment of Diseases of Children. By F. M. B. Allen, M.D., F.R.C.P., Physician, Belfast Hospital for Sick Children, Belfast. Eighth edition. Fabrikoid. Price $2. Pp. 268. Williams & Wilkins Company, Mt. Royal and Guilford Aves., Baltimore 2; Baillière, Tindall and Cox, 7 and 8 Henrietta St., Covent Garden, London, W. C. 2, 1947.

This book attempts to cover briefly the entire scope of pediatrics and to give aids to diagnosis and treatment. However, most of the material is inadequately covered, serious omissions are present and much of the material is obsolete. Intrathecal therapy is recommended for meningococcic meningitis, a procedure that has been discarded. None of the newer developments in the prophylaxis of rheumatic fever or the diagnosis and surgical treatment of congenital cardiac disease are mentioned.

There is little in the book that will be of aid to the student or practitioner.

Die Sauna: Ihre Geschichte—die Grundlagen ihrer Wirkung—ihre Anwendung zur Prophylaxe und Therapie mit einem Anhang: Bau und Betrieb der Sauna. Von Dr. Med. Victor R. Ott, Privatdozent an der medizinischen Fakulät Zürich. Cloth. Price, 15 Swiss francs. Pp. 224, with 29 illustrations. Grune & Stratton, Inc., 381 4th Ave., New York 16; Benno Schwabe & Co., Klosterberg 27, Basel, 1948.

The author states that one of the most important tasks of physical medicine is to submit well established physical procedures to an impartial scientific investigation.

The Finnish "sauna bath" became popular in Europe after the Olympics in 1936. At that time the Finnish athletes considered the regular use of "the sauna" to be so essential to their physical fitness that they had a sauna bath built in Berlin.

The sauna bath is a sweat bath heated by a stone oven in a small enclosed room. Basically it is a dry hot air bath, but steam is produced occasionally by sprinkling a small amount of water on the hot stones. Flagellation with birch twigs is done to promote hyperemia of the skin. Cooling is performed by a brief plunge into cold water.

Dr. Ott has compiled his data on the effects of the sauna bath over a period of several years.

A good review of the history of sweat baths through the ages precedes the discussion of the author's own experiences. The report is based on questionnaires sent to 95 healthy persons who used the sauna spontaneously, and on observations of 130 patients at the Polyclinic for Physical Therapy at the University of Zürich with varying complaints, predominantly rheumatic diseases and "neurovegetative" disturbances.

The physiologic effects observed include increases in bodily temperature, pulse rate, blood pressure and respiratory rate, electrocardiographic changes and changes in the chemical and cellular composition of the blood. The author also reports therapeutic effects by means of representative cases, but obviously a much larger clinical study would be required to prove the reported clinical results.

A comprehensive discussion of experimental physical conditions such as temperature and humidity of the air at various locations in the sauna room, heat radiation and cooling after the bath is included.

An appendix gives detailed specifications for the building and maintenance of a sauna bath.

The author has presented a thorough review of the subject and his experimental observations seem sound; however, his conclusions concerning clinical results, which include indications and contraindications for the use of the sauna bath, appear to be premature on the basis of his small series of cases. There seems to be little likelihood that this ancient and rather crude procedure will be employed extensively in American medicine, but physicians interested in modern forms of thermotherapy may find this presentation interesting.

Fundamentals of Human Reproduction. By Edith L. Potter, M.D., Associate Professor of Pathology, Department of Obstetrics and Gynecology, School of Medicine, University of Chicago, Chicago. Cloth. Price, $3.50. Pp. 231, with 92 illustrations by Alvin W. Meyer, F. A.A.R. McGraw-Hill Book Co., Inc., 330 W. 42nd St., New York 18, 1948.

This is an excellent reference or supplemental book for nurses on the subject of human reproduction. If used as a textbook it would require a skilled teacher, since there are none of the usual textbook appurtenances such as review questions, projects or other teaching helps. After the introduction, Part I proceeds in well planned sequence from a consideration of forms of animal life to the general pattern of reproduction, the factors responsible for body form and the number of offspring. Part II deals with the sex organs and their function, the development of the blastocyst and the formation of the placenta and a survey of embryonic and fetal development. In Part III, separate chapters are devoted to development of each of the following parts: brain and spinal cord, stomach and intestines, liver, pancreas, lungs, spleen, heart and blood vessels, kidneys and urinary bladder, organs of reproduction, glands of internal secretion, body framework, skin and accessory structures, and the face and sense organs. Part IV is devoted to birth and the future life of the infant.

There are excellent diagrammatic illustrations throughout the text. A notable feature is the series of photographs—twelve plates in number—which begins with the chorionic vesicle and

shows the embryo and fetus at various stages of development up to twenty-two weeks, including a roentgenogram of bony development at sixteen weeks. There are a good bibliography, a helpful list of visual aids and an adequate index. The book is well printed and attractively made. It can be recommended with enthusiasm for the use for which it was intended in nursing education or any other introductory course in embryology.

Introduction à l'étude de l'anesthésie: Chimie—biochimie—physiologie—physiopathologie—pharmacodynamie—thérapeutique—technique. Par L. Dautrebande, professeur à l'Université de Liége, E. Philippot, chef des travaux de thérapeutique expérimentale, et M. J. Dallemagne, assistant de chirurgie expérimentale. Précis des cours de l'Ecole d'anesthésie de Liége. Paper. Price, 750 Belgian francs. Pp. 1235, with 288 illustrations. Masson & Cie, 120 Boulevard St. Germain, Paris; J. Duculot, Gembloux, Belgium, 1944.

As the title implies, the book is an introduction to the study of anesthesia in all its aspects compiled with true continental thoroughness. It is dedicated, and is a worthy memorial, to Frank McMechan that good friend of the senior author (Dautrebande) and of all anesthetists. During the past quarter century the publications of the senior author, a distinguished Belgian physiologist, have been useful to American anesthetists. The book is divided into three parts. The first (410 pages) deals with the fundamental concepts of physiology, biochemistry and pharmacology which influence, and are influenced by, depressant drugs and the anesthetic state. The second part (150 pages) is concerned with the chemical, physical and other properties of anesthetic agents which influence the absorption and elimination of them by the body. The third part (379 pages) deals with the clinical applications of parts I and II. It includes details of all the various technics of administration, effects of various concentrations of the individual drugs, methods of determining concentrations and a general exposition of clinical anesthesia. Inhalational therapy, endotracheal technics and other subjects allied to anesthesia are dealt with quite adequately. Part III is, in itself, a textbook on clinical anesthesia. As such, however, it is slightly handicapped by an obviously limited clinical knowledge and experience of the authors. A very complete bibliography (244 pages) of the English and French literature and an index follow the text. The excellent table of contents appears at the end of the volume instead of at the beginning. This monumental work deserves translation into English. Meantime it will prove extremely valuable to those anesthetists and students who read French. The Belgian editor, J. Duculot, and the Paris printers are to be congratulated on the arrangement, printing and binding accomplished under wartime conditions. A paper-bound book of 1,235 pages which opens flat in the reader's hands and stands hard usage without falling apart is a triumph of the publisher's art.

Mental Health in Modern Society. By Thomas A. C. Rennie, M.D., Associate Professor of Psychiatry, Cornell University Medical College, New York, and Luther E. Woodward, Ph.D., Field Consultant, Division of Rehabilitation, National Committee for Mental Hygiene, New York. Cloth. Price, $4. Pp. 424. The Commonwealth Fund, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Square, London, E. C. 4, 1948.

This is a comprehensive and well written review of the social implications of modern dynamic psychiatry. The book deals particularly with developments in the field during and since the last World War. Included in its scope are factual and pertinent discussions of military psychiatry, the civilian readjustments required of the returned veteran, the role of the general practitioner in solving the problems of post-war rehabilitation and the contributions that can be made by social workers, psychologists, the clergy and by leaders in education and industry. Perhaps the only criticisms that can be made of this volume pertain to its implicit assumptions that much of the material it presents is of recent discovery, whereas in truth nearly all of the lessons we painfully "learned" during the last war were well known by 1920, were published in psychiatric journals and government reports, and were then tragically forgotten. Rennie and Woodward now remind us of the incalculable and protracted cost of war in human suffering and social turmoil, and we join with the authors in their fervent hope that this will be the last reminder we shall ever need. The book is highly recommended to physicians, social workers, clinical psychologists and all others interested in the field of social psychiatry.

Heart: A Physiologic and Clinical Study of Cardio-Vascular Diseases. By Aldo A. Luisada, M.D., Instructor in Physiology and Pharmacology, Tufts College Medical School, Boston. With a foreword by Herrman L. Blumgart, Physician-in-Chief, Beth Israel Hospital, Boston. Cloth. Price, $10. Pp. 653, with 353 illustrations. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, Maryland, 1948.

This text is written for the practitioner who desires to increase his knowledge of cardiovascular disease. It will be a valuable reference book also for medical students or postgraduate students reviewing this field. The field is covered competently; the book is well illustrated and has a very complete bibliography at the end of each chapter which includes not only the literature in English but also European references.

After a tabular history of cardiology and two chapters dealing with the development and function of the cardiovascular system, the author devotes two chapters to the clinical and technical (laboratory) study of the patient. The author has abandoned the usual etiologic presentation of the heart diseases and substituted an anatomical-clinical classification which he attempts to correlate with etiology. To the reviewer this seems only to lengthen the volume without achieving any clarification of diagnosis. The author complains in his preface that the etiologic classification of heart disease has resulted in mental laziness in formulating an exact diagnosis. Nowhere in his book does he stress that an adequate diagnosis of cardiovascular disease should include a statement of the etiologic factor, the anatomic lesion and the physiologic disturbance, as well as a functional and therapeutic classification. The latter two are becoming more important, especially in connection with patients who are recommended for rehabilitation and employment.

In general one can concur with the majority of his statements regarding diagnosis and therapy. A few topics on which some discussion would be expected are either omitted or only briefly mentioned. These are: the use of anticoagulants in coronary thrombosis with myocardial infarction; the low sodium diet in hypertension, and the use of penicillin in cardiovascular syphilis.

Bergey's Manual of Determinative Bacteriology. By Robert S. Breed, E. G. D. Murray and A. Parker Hitchens. Assisted by Sixty Contributors. Sixth edition. Cloth. Price, $15. Pp. 1529. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, 1948.

The new sixth edition of this standard reference, revised under the editorial chairmanship of Robert S. Breed, contains contributions from sixty well known specialists in the field of bacteriology. Changes in the presentation and relationships of almost every genus of bacteria have been made by specialists in consultation with the editorial board. Nearly three hundred new species are described. Because of increased knowledge the number of species described under fission fungi has increased from 1,335 in the fifth edition to 1,630 in the present manual.

The authors state that the present edition does not cover all the descriptions of species found in the literature for, as in all other branches of biology, many of the descriptions are so inadequate that the species described cannot now be identified. Additionally, many of the descriptions are obvious duplications of previous descriptions, while other so-called differences are based on nothing more substantial than the investigator's opinion. A completely new feature, the "Source and Habitat Index," has been added to this volume; the editors believe that it will be extremely useful both to teachers and investigators in determining the identity of a described species or whether a given species is new. Organisms cannot be classified before detailed study of their morphologic, cultural, physiologic and pathogenic characters is made, and the student is warned not to take too literally the descriptions which are drawn to represent average findings. Especially among bacteria, characters such as sugar fermentations, gelatin liquefaction, presence or absence of flagella or other identifying characters may vary.

New information for this volume has been taken from dark field motion pictures of motile cells and photographs taken with the recently developed electron microscope, revealing heretofore unsuspected facts regarding structural features. The book contains a wealth of references to both the domestic and foreign literature for the use of the student and investigator. The total number of pages of the book has been increased from 1,031 to 1,529. Additionally, each page contains approximately 20 per cent more material than the pages of the fifth edition. The structure of the contents of the book remains essentially the same.

Principles of Medical Statistics. By A. Bradford Hill, D.Sc., Ph.D., Professor of Medical Statistics in the University of London, London. Fourth edition. Fabrikoid. Price, 10s. 6d. Pp. 252, with 13 illustrations. The Lancet Limited, 7 Adam St., Adelphi, London, W. C. 2, 1948.

The preface to this fourth edition remarks that the book was written primarily to introduce the worker in clinical medicine as gently as possible both to statistical ways of thinking and to simple statistical methods of experimentation and analysis. The gentleness is manifest in an almost complete absence of mathematical symbols other than signs for multiplication, division and root extraction. Any one who retains a slight command of his high school algebra, specifically the binomial theorem, will be able to understand everything in this book provided that he is willing to contribute the needed time and effort.

One or two slight peculiarities remind the reader that mathematics is not yet quite the universal language. Some American readers may need to be reminded that in British publications the symbol 7·23 with the dot above the level of the line does not mean the product of 7 and 23 but the sum of 7 and 23/100. It is also noted that the Fahrenheit scale of temperatures is used throughout. It is earnestly to be hoped that this will soon be replaced everywhere by the Centigrade scale.

The methods for computing chi square for fourfold tables and of the correlation coefficient for ungrouped and grouped data are well explained. Considerable space is given to death rates and life tables. There are three chapters on common fallacies and difficulties, and a concluding chapter on "Common Sense and Figures" takes much of the wind out of the sails of unbelievers in statistics.

A slight expansion of the index with appropriate changes in the text would make the book more useful to readers who wish to know the meaning of "tetrachoric" and "root-mean-square." Some terms like these are not represented in the index, though their equivalents can be located in the text if one already knows what they mean. In general, however, the omission of many important aspects of statistical science is explained by the fact that they simply do not admit of elementary presentation. If this is kept in mind, the book should be extremely useful. In particular, the section on questionnaires will help many an investigator to avoid trouble, and a copy of this book should be available to every one planning clinical research.

Experimental Air-Borne Infection: Equipment and Methods for the Quantitative Study of Highly Infective Agents; Basic Data on Their Use Obtained with Phenol Red, Serratia marcescens and Bacillus globigii; and Preliminary Experiments on the Stability and Infectivity for Laboratory Animals of Air-Borne Clouds of Brucella suis, Malleomyces mallei, Malleomyces pseudomallei, Pasteurella tularensis, and of Viruses of the Psittacosis Group. By Theodor Rosebury. With the co-authorship and assistance of the Staff of the Laboratories of Camp Detrick, Maryland. Microbiological Monographs [1]. Official Publication of the Society of American Bacteriologists. Cloth. Price, $4. Pp. 222, with 45 illustrations. Williams & Wilkins Co., Mount Royal & Guilford Aves., Baltimore 2, 1947.

This first Microbiological Monograph of the Society of American Batteriologists presents results released by the Biological Warfare Service on investigations of experimental air-borne disease. The work was forecast in the original proposal of a project, published in the *Journal of Immunology* a few months ago. Between December 1943 and October 1945 Dr. Rosebury, with eleven co-authors and sixteen mentioned assistants, conducted investigations on air-borne infection at Camp Detrick, Maryland. Disease was induced in small animals by inhalation of droplet nuclei aerosols of Brucella suis, Psittacosis virus (Borg), Psittacosis virus (6BC), Malleomyces pseudomallei, Malleomyces mallei, Meningopneumonitis virus (Cal 10) and Pasteurella tularensis; the report does not indicate whether the list is complete but states,". . . work with infective agents was begun 21 March, 1945, and continued until shortly after the end of the war." These protocols occupy one tenth of the volume.

The remaining nine tenths of the book records the procurement of equipment and secret training for a study of experimental air-borne disease. The first part describes elaboration of apparatus for safe exposure of animals to aerosol suspensions of virulent organisms in droplet nuclei. The second describes certain selected atomizers for producing infective aerosol clouds. The third part discusses their modification of the Greenburg dust impinger for bacterial sampling. Since alteration of critical dimensions sacrifices impinging efficiency, the authors state: ". . . the sampler operates as a bubbler rather than as an impinger in the strict sense." Bubblers are much less efficient collectors of droplet nuclei than impingers, but the violence of this type of impinger may, by destroying fragile organisms, as the authors suggest, perhaps account for the small lethal dosages (one third) obtained by British investigators of Biological Warfare. In air bacteriology quantitative precision is illusive.

Nevertheless, the mortality patterns parallel previous results on air-borne influenzal and streptococcic infection of mice in that geometric increases in dosage tend to yield arithmetic increases in mortality, but dosage *par quantum* of infection is much higher than for air-borne tuberculosis in rabbits. The work adds valuable new evidence on the vulnerability of animals to inhaled droplet nuclei infection. Though, according to the naval unit in California, from studies on droplet nuclei infection in which similar equipment was used: "The preliminary studies on the apparatus were carried out with Pasteurella pestis," neither mentions experimental air-borne pneumonic plague. Perhaps omission of such an apparently obvious agent of air-borne infection could also be significant.

The Danish Cancer Researcher, Johannes Fibiger, Professor in the University of Copenhagen. By Knud Secher, Physician in Chief to the Bispebjerg Hospital, Copenhagen. Paper. Pp. 206, with illustrations. H. K. Lewis & Co., Ltd., 136 Gower St., London, W. C. 1; Nyt Nordisk Forlag, Arnold Busck, Kjøbmagergade 49 [1], Copenhagen K, 1947.

This interesting biography of Prof. Johannes Fibiger, the Danish pathologist, was written by an assistant, Knud Secher. The introduction deals with the family background which is traced back as far as Gotfried Fibiger (1665-1719), the court trumpeter. A chapter on his childhood and youth is followed by an account of his early training. This was the period of awakening of Danish medicine and the era of such figures as Pasteur, Virchow, Paget and C. Lange. In 1891 Fibiger had already studied under R. Koch in Berlin. In 1900 he was appointed professor of pathologic anatomy in the University of Copenhagen, where he became deeply interested in undergraduate teaching and subsequently (1925-1926) served as Rector of the university. His scientific career is marked by his interest in diphtheria in his youth and later in tuberculosis and cancer. His researches on tuberculosis were high lighted by the historic controversy with Koch on the significance of bovine tuberculosis in human beings. A large part of the book deals with his interest in cancer, especially his well known studies on cancer of the stomach in rats. Here the author gives an accurate and detailed account of the various steps in this research leading to the discovery of Spiroptera neoplasticum, a parasite of the cockroach, as a probable cause of benign and malignant changes in the rat's stomach. This work was first published in 1913 and won for him the Nobel Prize in medicine in 1927. Then follows an account of the difficulties surrounding the repetition of these experiments by other investigators as well as the main lines of criticism. In this discussion the author is conservative throughout and makes no undue claims as to the ultimate significance of Fibiger's contributions. The book is well written and holds considerable value for students of medical history. For those interested especially in experimental cancer, the book gives an authentic account of an interesting era in the history of cancer research.

Laws, Rules, Regulations Relating to Tuberculosis, California, Arranged by Topic. Compiled by Mary Graham Mack. Paper. Price, $2. Pp. 250. National Tuberculosis Association, 1790 Broadway, New York 19, 1947.

The National Tuberculosis Association has undertaken to compile for each state, territory, the insular possessions and the District of Columbia, the laws, rules and regulations relating to tuberculosis and will publish them in separate pamphlets. These pamphlets will serve as a basis for comparative legal studies on various related topics, including isolation and quarantine of recalcitrant patients, establishment and control of sanatoriums, vocational rehabilitation and administrative functions of official agencies. One objective of this study is the formulation of model and uniform laws to reconcile the differences now existing. The pamphlet here reviewed, covering California, has recently been completed. Others will follow.

The Efficient Dental Assistant. By Ethel Covington, D.H. Second edition. Fabrikoid. Price, $3.50. Pp. 285. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

This book is planned to make life easier for dentists who employ untrained assistants, to relieve the first few weeks of utter confusion experienced by many girls, and to provide some new ideas and fresh enthusiasm for assistants who have been in dental offices for a number of years.

The second edition includes a new chapter on "A Personality Formula for a Successful Dental Assistant."

In the first chapter, "Your Speech Personality," the author explains the proper method of answering the telephone or greeting a patient, and stresses the fact that an assistant can be a builder or a destroyer of good will merely by the tone of her voice or her manner. The "hundred and one little things" in personal habits and manners which may prove offensive and annoying on repetition are cleverly presented. The third chapter is devoted to the duties of a dental secretary or office manager and includes an outline for dental bookkeeping and valuable information on writing professional letters. The chapter on "Professionalizing the Office" defines clearly the armamentarium and uses of medicine, materials and supplies in any dental office. In the following chapters, sufficient information is presented to acquaint a beginner with dental terminology, the processing of roentgenograms, G. V. Black's classification of cavities and the ages at which various teeth erupt.

Atlas of Plastic Surgery. By Morton I. Berson, M.D. Fabrikoid. Price, $15. Pp. 304, with illustrations. Grune & Stratton, 381 Fourth Ave., New York 16, 1948.

Berson's book stresses the technic of certain plastic procedures by way of numerous illustrations, leaving little space for text. Since it is impossible to do full justice to both within the limited confines of one volume (303 pages) the work fails to attain its objective, which the author states is to "furnish a clear exposition of the surgical procedures for postgraduate student, the general surgeon and the specialist. Nothing has been sacrificed for the sake of brevity."

Obviously it was possible for the author to describe only a limited number of procedures, and his choice in some instances is open to question.

The drawings for the most part are extremely good, but some of the illustrations, particularly photographs showing technical details, are not as clear as they might be.

The book will be of some value in connection with other works which discuss indications, postoperative care and complications but can hardly be considered adequate in itself.

Psychobiology and Psychiatry: A Textbook of Normal and Abnormal Human Behavior. By Wendell Muncie, M.D., Chairman, Medical Advisory Board, Seton Institute, Baltimore. Second edition. Cloth. Price, $9. Pp. 620, with 70 illustrations. C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1948.

The first edition of this book was published in 1939. Obviously psychiatry has undergone a revolution since that time, so that extensive revisions of the book became necessary. The volume is designed primarily for the instruction of students. Indeed, it gives opportunity for the student to make a psychologic evaluation of himself according to a variety of tests now in common use. There are many clinical devices fully elucidated. Thereafter is a consideration of a psychoneurosis and other forms of mental disturbance with excellent clinical reports. Mental difficulties are evaluated as depressions, elations, illusional states, convulsive states and organic deficit reactions. In the present experimental stage of psychiatric study and education, the book offers a reasonably well oriented guide for the general practitioner.

The Metabolic Brain Diseases and Their Treatment in Military and Civilian Practice. By G. Tayleur Stockings, M.D., B.S., D.P.M. Cloth. Price, $4.50. Pp. 262, with 3 illustrations. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, Maryland, 1947.

This treatise on the metabolic diseases of the brain and their treatment is primarily written for psychiatrists and discusses, in a rather unusual way, all forms of shock treatment for mental disease. The author feels that this work will answer two important questions. They are: 1. What is the pathophysiologic basis, if any, of the conditions known generally as the schizophrenic, delusional and affective psychoses? 2. What is the physiologic and chemical mechanism of the insulin and shock therapies? This book is the result of studies made on several hundred acute and typical cases of mental disease treated by the writer during the last five years. There are fifteen chapters starting with an introductory part and ending in a chapter on conclusions with a scheme of classification of mental disease and a bibliography. The author introduces an entire new scheme of disease nosology and classification which is less practical than the old classifications. The writing is clear and concise. There are so many controversial ideas discussed here that enumerating them would require considerable space. This book should be in the library of all psychiatrists and teachers of psychiatry. It is of no value to students and general practitioners.

Méthodes statistiques en médecine et en biologie. Par E. Morice, professeur à l'Institut de statistique de l'Univertité de Paris, Paris. Avec la collaboration de M[lle]. M. Tisserand et du D[r]. J. Reboul, professeur agrégé à la Faculté de médecine de Lyon, Lyon. Préface du professeur A. Baudouin. Paper. Price, 480 francs. Pp. 181, with 53 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris, 6[e], 1947.

This book attempts to describe a majority of the technics of statistical methodology which have proved useful in medical and biologic research. Its general procedure is to outline briefly the assumptions behind each method or formula, to describe the application and necessary calculations and, finally, to draw the indicated conclusions. It omits almost all derivations. This omission is a commendable feature of a book primarily designed for the physician. Aside from the fact that it is written in French, it can be understood by a reader with a minimum amount of mathematical training.

The first portion of the book includes the usual topics such as classification, graphic representation, measures of central tendency, dispersion and symmetry. It omits any mention of the harmonic and geometric means. The binomial, normal and Poisson distributions are briefly described. Tests of significance are considered in the latter portions of the book. Unfortunately, no mention is made of the F test of Snedecor or its equivalent, the z test of Fisher. An adequate treatment is given for each of the other common tests.

A satisfactory treatment of simple correlation is followed by an inadequate treatment of partial and multiple correlation. Unfortunately, no mention is made of the standard error of estimate. A more extensive treatment of regression should have been included. A short description of time series problems is included. The restriction of this subject is commendable, since an adequate analysis of time series would demand a complete book by itself.

An interesting discussion of the methods of collection of data and experiment design in medical research is included. The book closes with a brief but interesting treatment of certain fundamental concepts of mathematics needed in statistics.

Internal Medicine in General Practice. By Robert Pratt McCombs, B.S., M.D., F.A.C.P., Assistant Professor of Medicine and Director of Postgraduate Teaching, Tufts College Medical School, Boston. Second edition. Cloth. Price, $8. Pp. 741, with 122 illustrations. W. B. Saunders Co., 218 W. Washington Sq., Philadelphia 5, 1947.

The second edition of this deservedly well known book has retained in its general plan the form of the first edition in that, as well described in the preface, the basic principles of everyday problems in internal medicine have been factually reviewed, whereas controversial material and discussions of diseases only rarely encountered in the United States as well as discussions of technical procedures lying solely within the province of the specialist have been much condensed or omitted entirely. Throughout the book it would seem that diagnostic and therapeutic methods most readily adaptable for use in general practice have been stressed and the effort has been made within the limits set by the relatively small size of the volume to review and integrate the physiologic principles underlying these methods with discussions of the clinical aspects of the diseases in which they are employed. Much new and timely material has been added in the preparation of this second edition, and short selected bibliographies are appended at appropriate places. The second edition of Dr. McCombs' book should be, like the first edition, most useful to the busy general practitioner.

Treatment by Diet. By Clifford J. Barborka, B.S., M.S., M.D., Assistant Professor of Medicine, Northwestern University Medical School, Chicago. Fifth edition. Fabrikoid. Price, $10. Pp. 784, with 14 illustrations. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1948.

Much of the recent voluminous literature on nutrition has been revised and significant additions have been incorporated in the fifth edition. Tables summarizing the effects of vitamins on the body, sources of supply and recommended daily allowances give much information in a concise form. Other tables give analysis of foods that serve to meet basic requirements, symptoms of deficiency states, conditions that influence vitamin requirements and utilization and other significant data. In general, tables are well constructed, clear and contain sound current information. A number of excellent colored photographs add considerably to the value of the book. Seven photographs show comparative servings of foods in such a clear manner that they should be helpful to the physician in diet prescription. Effects of deficiency diseases are shown in three colored photographs and experimental studies in humans on a deficient vitamin C diet clearly show alterations in the healing pattern of wounds.

All the more common disease entities that have nutritional problems are briefly discussed. A number of suggested diets and supplementary instruction for patients form a valuable part of the book. The chapter on cutaneous disease and diet summarizes recent knowledge in the field. A large appendix containing many useful tables, weights and measures and recipes adds to the usefulness of the book. The extensive bibliography is helpful in finding original articles. A good table of contents and index make it easy to find subject matter, although it is disappointing that there is no index of the beautiful colored photographs. On the whole the book is well written, suitably illustrated and can be recommended to physicians interested in the dietary treatment of disease.

Pathological Histology. By Robertson F. Ogilvie, M.D., F.R.C.P., F.R.S.E., Lecturer in Pathology and Assistant in Forensic Medicine, University of Edinburgh, Edinburgh. Foreword by A. Murray Drennan, M.D., F.R.C.P., F.R.S.E., Professor of Pathology, University of Edinburgh. Third edition. Cloth. Price, $10. Pp. 459, with 260 illustrations. Williams & Wilkins Co., Mt. Royal & Guilford Aves., Baltimore 2, Maryland, 1947.

In the recently published third edition of this book, much of the text is said to have been revised and expanded and fifteen new subjects and their illustrative plates added. The quality of the book, however, remains unchanged. Most of the illustrations are excellent examples of the pathologic processes which they illustrate. The color photography excels the photomicrographs in most medical textbooks made in this country, although overstaining with eosin detracts from the beauty of many of the preparations. If this book were to be used as an atlas of pathologic histology and not as a textbook of pathology, it could be useful to American students in medical schools where classes are large, instructors are few and material limited in quantity or quality. Although this book is not intended to replace standard textbooks, its conciseness and attractiveness seem to offer the time-harried student a way out of his perennial dilemma. Unfortunately, however, textual material is inadequate for this purpose, and, aside from the gross and microscopic descriptions, the text is so limited in scope that it might be better to omit it and make the book entirely a laboratory atlas. This would increase its real usefulness to students and at the same time would decrease both the bulk and the cost of the book.

La chirurgie biliaire sous contrôle manométrique et radiologique per-opératoire. Par Pierre Mallet-Guy, professeur à la Faculté de médecine de Lyon, Lyon. René Jeanjean, Assistant à la Faculté, et Pierre Marion, Chef de Clinique à la Faculté. Paper. Price, 1200 francs. Pp. 138, with 170 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1947.

This well documented discussion of cholangiography—the materials needed, the technic, the indications and the interpretations of manometric and radiologic procedures to be carried on concurrently with the surgical treatment of the biliary tract deserves careful study. The procedure is not new, having been given its great first impetus by Mirizzi, of Cordoba, Argentina, who in 1939 published a monograph on the subject. The text is based on 550 operative cases. The authors' technic has been somewhat simplified by the use of a portable, completely enclosed x-ray machine on wheels, sufficiently small to be wheeled under the operating table. The operating table itself is of unique pattern, supported at the two ends instead of by a central pedestal, thus permitting the placement of the x-ray apparatus under the operating table. A device is provided which permits quick simultaneous centering of the x-ray tube and the film holder in the midst of the operation. The authors consider carefully the problems of anesthesia incident to surgery in the presence of x-ray equipment. Numerous beautifully reproduced illustrations are accompanied by explanatory line drawings which make them perfectly clear to the reader. This book is worth while.

You Can Be Thin! Slenderness Through Psychology. By Herman Friedel, M.D. Foreword by Milton Jacovy, M.D. Fabrikoid. Price, $2. Pp. 117. Caxton House, Inc., 9 Rockefeller Plaza, New York 20, 1948.

Another booklet about weight control with the usual diet lists, tables of caloric content of the common foods and, as an innovation in the popular literature of this field, with emphasis on the importance of psychological factors—such as inner conflicts and frustration—in the development of obesity. This will hardly suffice to increase the number of persons who can reduce their weight to or below normal through their own efforts, as promised in the title of this booklet. But it may be useful education for the obese subject if it helps him to understand why his physician tries to explore his personal problems as part of his examination and treatment.

Motivation in Health Education: The 1947 Health Education Conference of the New York Academy of Medicine. Cloth. Price $1. Pp. 53. Columbia University Press, 2960 Broadway, New York 27, 1948.

Four qualified contributors present a well rounded clinical analysis of the basic problems of health education and how these may eventually be resolved. Every health educator will encounter in each of the contributions numerous examples of problems with which he or she has wrestled, often despairingly. These matter of fact introspections are both refreshing and encouraging. They demonstrate that health education is not the intangible, formless problem that many are apt to consider it but a living, pulsing subject closely interwoven with all human activities. Physicians as well as lay workers in health education will obtain helpful orientation through consultation of this volume.

Confrontations radio-anatomo-cliniques. II. Publiées sous la direction de M. Chiray, R. A. Gutmann, et J. Sénèque. Paper. Price, 465 francs. Pp. 69, with illustrations. Gaston Doin & Cie, 8 place de l'Odéon, Paris 6e; Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1947.

A previous review in these pages concerned volume I of this series of 42 case reports. The reviewer is favorably impressed with the choice of the cases and the complete analysis of the roentgenologic, anatomic and clinical aspects. Differential diagnosis is thoroughly considered. Many of the cases are gastroenterologic, but a number of documents relate to osseous pathology. The photographs of the anatomic specimens add to the value of the presentations. This series of "dry clinics" is presented on a high plane of scientific excellence.

Healing Herbs of the Upper Rio Grande. By L. S. M. Curtin. Boards. Price, $7.50. Pp. 281, with 30 drawings by P. G. Napolitano. Laboratory of Anthropology, Santa Fe, N. M.; San Vicente Foundation, Inc., 984 Acequia Madre, Santa Fe, N. M., 1947.

This book contains a series of brief discussions on articles ranging from Mexican oil (aceite mexicano) to love-vine (yerba mala) arranged alphabetically according to the Spanish name. If the book is not accepted as a therapeutic guide it offers some rather unusual bits of information presented in a somewhat popular style. This is essentially a collection of statements on primitive herbal medicine.

Some Fundamental Principles of Metabolism. By L. H. Newburgh, M. W. Johnston, and J. D. Newburgh. Third edition. Paper. Price, $2. Pp. 70, with 20 illustrations. J. W. Edwards, Ann Arbor, Michigan, 1948.

This monograph offers to physicians some basic knowledge of the manner in which the body uses food and water. The physics and chemistry concerned are beyond the depth of most practicing physicians; yet a basic knowledge is essential, particularly in controlling such conditions as obesity, undernutrition, edema and fever.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

METHYL ALCOHOL INTOXICATION

To the Editor:—**Recently I was asked to testify on the effect of methyl alcohol on a man. Please furnish the additional needed information. The patient was an apparently healthy man about 45 to 50 years old. He had had several teeth extracted shortly before being arrested for drunkenness and had taken acetylsalicylic acid ("empirin") tablets for pain. He had taken whisky during the previous evening and the morning of his arrest. About noon that day he drove his car about 60 miles. His car contained "zerone" antifreeze. "Zerone" contains 90 per cent methanol (methyl alcohol). The odor of the antifreeze was strong in the car, especially when all the windows were closed and the heater (hot water type) was turned on. When he was arrested, at about 3 p. m., the arresting officers stated that he was so drunk that he could not stand up, his speech was slurred and he had to be assisted to the jail. About one hour later he was released from jail, and at that time was able to write his name when he posted his bond. He recognized the difference between a one dollar bill and a five, and could walk straight without assistance. Have cases of intoxication occurred from inhaling methyl alcohol antifreeze? Would the fact that he had taken some whisky make the effect of the fumes greater? Would the effects of the whisky, antifreeze, and acetylsalicylic acid have caused him to be more stuporous than whisky alone? Does the presence of whisky (ethyl alcohol) in the body slow down combustion of methyl alcohol? V. Fallenberg (Sollman, Manual of Pharmacology, 1936, p. 682) stated ". . . if methyl is mixed with ethyl alcohol, as in liquors, the combustion is incomplete, and harm results from relatively small doses." Would a man as drunk as the arresting officers said that he was have been able to recover from whisky intoxication as quickly as he apparently did?**

Joseph W. Chinn, M.D., Tappahannock, Va.

ANSWER.—The extraction of the teeth may have interfered with his driving, particularly since he may have been given procaine hydrochloride with epinephrine. The acetylsalicylic acid would not have effect on his condition unless it had been taken with codeine, and even then the chances are that the effect would have been negligible. The alcohol which he imbibed the night before was probably eliminated before noon the next day. However, the alcohol that he took the next morning would most likely have been present in his blood at noon and possibly for several hours thereafter.

The inhaling of alcohol fumes definitely increases the amount of alcohol in the blood. An instance is known of considerable discomfort and disorientation caused by sitting in a car filled with alcohol fumes. A specimen of urine taken about an hour afterward revealed 0.025 per cent alcohol, which is about the amount that one would have had from an ordinary "shot." Intoxication from the inhaling of methyl alcohol is a definite possibility.

It is likely that the subject was under the influence of ethyl alcohol before he inhaled the methyl alcohol fumes. It is fairly well established that methyl alcohol is less poisonous than ethyl alcohol if the methyl alcohol can be prevented from being oxidized to formic acid. Røe explained that ethyl alcohol in the stomach prevents absorption of ingested methyl alcohol. Also, formic acid ordinarily produced by the oxidation of methyl alcohol will not be formed when ethyl alcohol displaces methyl alcohol in the respiratory organs. In the medicolegal case under discussion, it seems that the subject had consumed the antidote before he was exposed to methyl alcohol. There is, therefore, little likelihood that the methyl alcohol inhaled was an important factor in his state of intoxication. The acetylsalicylic acid would have had no effect on his condition unless toxic doses had been taken, and evidence is lacking that such was the case. The apparent quick recovery is not typical of methyl alcohol poisoning, but commonly occurs when a person is sufficiently stimulated by his surroundings to become temporarily sober.

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TINEA CAPITIS

To the Editor:—**Two small boys, ages 7 and 9, have tinea capitis. They have been under the care of a dermatologist for four months. The Wood light shows that the infection is still active. The mothers are intelligent and cooperative, the hair is kept closely clipped and thoroughly scrubbed every night and the salve applied as directed by the dermatologist. What further treatment can be given to hasten cure of their infection?**

Eva Cutright, M.D., Wooster, Ohio.

ANSWER.—Tinea of the scalp may be treated by either roentgenologic epilation, manual removal of infected hairs, topical applications or combinations of the three methods. None of these provides a rapid cure, and the choice of method employed depends in large part on the circumstances in each case. It is desirable first to identify the organism from culture, for tinea capitis due to Microsporum lanosum usually responds readily to treatment by manual removal of infected hairs and topical applications, whereas that due to Microsporum audouini is rather resistant to such therapy. Topical therapy alone is usually adequate when there is pustular involvement of the scalp.

If in the aforementioned instances there are no other children at home who might become infected and if the youngsters can be trusted to protect their playmates and schoolmates by wearing caps constantly and not exchanging them, it would be well to continue with conservative treatment, which is the application once or twice daily of an ointment of 5 per cent salicylanilide in "carbowax 1500" over the entire scalp followed every few days by a thorough washing of the scalp with tincture of green soap. After the shampoo, when the scalp is free of ointment, it should be examined under the Wood light and all infected hairs removed with a tweezer. These hairs can be detected easily, for they assume a bright green color under the Wood light. If there is not sufficient improvement after a few weeks with this treatment, epilation may then be accomplished by means of roentgen therapy. The technic is exact and must be executed with skill and caution. In one sitting an epilating dose of roentgen rays is administered to the entire scalp with the five point method of Kienbock-Adamson. In three weeks the hairs and with them the fungi begin to fall and, with the use of strips of adhesive tape, those hairs which still adhere are removed. The scalp then should be examined under the Wood light to detect the presence of any scattered infected hair stubs, which should be extracted so that the scalp is entirely bald. An antiseptic ointment, such as salicylanilide, ammoniated mercury or sulfur, should be applied daily during this period until there is a regrowth of hairs. New hairs begin to grow in again after one to three months. The new hair is usually vigorous. On rare occasions the new hairs may differ in quality from the old—they may be straighter or more curly, finer or coarser in texture, and they may even change a little in color. The new hairs should be examined with the Wood light at intervals for several months.

In experienced hands, the treatment of tinea of the scalp by roentgen epilation has proved safe and reliable in thousands of instances. But it must be emphasized again that the treatment is an exact one to be administered with caution. It should be used only by one skilled in the use of roentgen rays for epilation of the scalp if permanent ill effects are to be avoided.

COLD ALLERGY

To the Editor:—**Several of my patients suffer from respiratory allergic attacks precipitated by contact with cold air. Is it possible to desensitize these people to cold?**

M.D., Connecticut.

ANSWER.—While attacks of asthma are frequently precipitated or aggravated by exposure to cold, patients in whom this is the primary immunologic cause of such attacks are unusual. Such patients usually have other manifestations in addition to nasal and bronchial symptoms on exposure to cold. Urticaria and angioneurotic edema are not only the most frequent associated manifestations but generally the main or only manifestations of cold allergy. In addition, various degrees of prostration associated with a sudden fall in blood pressure may occur when the exposure is sudden and the surface area chilled is extensive.

The cases mentioned by the inquirer are probably not primary cold allergy. Patients who are sensitive to inhalants and have symptoms of either nasal allergy alone or bronchial and nasal allergy are not uncommonly intolerant of cold. This is generally due to the irritating effect of cold air on a labile and irritated mucous membrane which responds rapidly to all types of nonspecific irritants (smoke, odors, inorganic dust) with increased edema and therefore increased nasal or bronchial obstruction. Treatment of asthma precipitated by cold depends

on the determination of whether the symptoms of asthma are due to primary cold allergy or to the more common effects of nonspecific irritation (Urbach, E., and Gottlieb, P. M.: Allergy, New York, Greene and Statton, 1946, pp. 411-415; Cooke, R. A.: Allergy in Theory and Practice: Philadelphia, W. B. Saunders Company, 1947, pp. 482-485).

Primary cold allergy is extremely difficult to treat. The simplest treatment, suggested by Horton and Roth of the Mayo Clinic, is the immersion of the hands or arms in cool water for one or two minutes twice daily. The temperature of the water is gradually lowered from 65 degrees F. until the patient is able to tolerate water at a temperature of 45 degrees F. Ice rubs or cool showers have been suggested by some allergists. Other methods depend on increasing the patient's tolerance of histamine by daily injections of small doses of the drug, gradually increasing the interval of injections to once a week. Antihistaminic drugs have recently been suggested in doses of 50 to 100 mg. every four hours as needed. These and numerous other measures reviewed in the textbooks mentioned are rather lame suggestions for therapy of a most difficult condition. The results are seldom good in cases of asthma due to primary cold allergy.

As for the more commonly encountered condition of intolerance to cold on a nonspecific basis in patients sensitive to inhalants or occasionally to foods, the treatment depends primarily on the cause of the respiratory allergy. Inhalants to which the patient is clinically sensitive should be removed from the patient's environment if possible. If this cannot be accomplished satisfactorily (as in sensitivity to pollen, mold and house dust), treatment by increasing the tolerance through injections of the antigens is necessary. Foods to which the patient is sensitive should be eliminated from the diet. The more successful the treatment of the primary allergy the less will nonspecific irritants affect the respiratory mucosa. Meanwhile the patient should be protected by adequate clothing during cold weather. Commonly such patients protect the mouth and nose by the use of a scarf to avoid breathing cold air.

NUTRITION IN ILLNESS

To the Editor:—**I am involved in a discussion on the type of nutrition most appropriate during acute illness, particularly febrile illness. Both sides agree that protein is necessary but disagree on type. One side maintains that as much meat and eggs should be given as the patient can tolerate without inconvenience, as those proteins are most complete for rebuilding of tissues, and that vitamins should be given in abundance. The other side maintains that protein should be given only as milk and vegetables to prevent overstimulation of metabolism by excess protein and also to avoid the toxic effects of nuclear proteins and nucleic acids. It also asserts that vitamins should be given sparingly to prevent invading micro-organisms from receiving the benefit of growth stimulation. What are the exact reasons for restriction of meat in certain diseases, such as nephritis?**

M.D., Canada.

ANSWER.—The acute period of a febrile illness such as pneumonia is usually of such short duration that the nutrition problem is chiefly one of nutrient fluids which may be taken with a minimum of effort on the part of the patient and with emphasis on the liquid rather than on the protein. Milk and orange or other fruit juices have been judged most suitable at this stage. As soon as the acute stage of fever is past, generous amounts of protein should be fed to check its rapid loss and to prevent hypoproteinemia. A variety of tender meats, eggs and milk supplemented by cereal and vegetable proteins should be used. At least 1 Gm. of protein per kilogram of body weight should be given, this being increased up to 1.5 or 2 Gm. per kilogram if serum proteins are already low, until normal serum protein levels are reached. The added growth requirements of children may bring the levels needed for them up to 4 or 5 Gm. per kilogram of body weight as shown by Harrell for children with Rocky Mountain spotted fever. The relation of protein to antibody formation reported by Cannon suggests a further reason for maintaining adequate protein levels as a protection against infection.

Vitamins should not be restricted in infections. Any condition such as fever which increases metabolism increases the requirement for thiamine. In tuberculosis generous intake of ascorbic acid is necessary to maintain normal plasma levels and appears to reduce the extension of infection to the digestive tract. The incidence of deficiencies of nicotinic acid and riboflavin in patients was also found higher than average. The observation that vitamin A tends to disappear from the blood during fever and the favorable results with the use of vitamin A in animals with tuberculosis indicate that it should not be restricted in infection.

The exact reasons for restriction of meat in nephritis are not obvious. Possibly the more severe effects of large quantities of meat protein on rat kidneys compared with the simple hypertrophy found with equal levels of casein have influenced some. In other cases, no doubt, such restriction is used as a simple way of reducing protein intake. Meat also is acid forming, and the use of basic diets in nephritis has received some favorable reports. Protein consumption should not be reduced below the minimum metabolism. This with adequate intake of energy may approximate 0.5 Gm. per kilogram of normal weight. Lower intakes would not spare the kidney and would deplete body protein. In the nephrotic syndrome the protein intake should equal the minimum metabolism plus the albumin excreted plus enough to build the depleted serum protein up to normal.

ARTERIOSCLEROSIS AND DIABETES

To the Editor:—**A physician 88 years of age, a recognized early authority in roentgenology, has been diabetic for years and is now suffering from the vascular changes that may take place in the advanced years: arteriosclerosis, hypertension, vascular spasm—but no visible retinal hemorrhages. He has macular degeneration of the left eye and has had an embolus that first involved the central retinal artery of the right eye and blocked lower retinal arteries, thus resulting in a blind upper field but with preservation of reading vision in this eye. Other vascular involvements of the lower extremities have occurred but his brain has remained clear. He has circulatory impairment which involves the right lower extremity when suddenly assuming sitting or erect position. While lying down he is able to move the lower extremity at will, but when erect the right leg is somewhat paretic, at times causing him to fall. Most of the time while erect he favors it by support and by chair to chair progress. He has become interested in the possibilities of ether as a therapeutic agent in the terminal stages of arteriosclerosis. I have been able to obtain only short, incomplete references to the use of ether. What are the references stating amount or frequency of dosage and possibility of its use intramuscularly?**

Alfred Dean, M.D., Grand Rapids, Mich.

ANSWER.—The condition described by the correspondent is naturally an irreversible process of advanced cardiovascular disease which fortunately has left the mental capacities intact. There are obviously multiple arterial occlusions in various segments of the vascular tree. The lesion in the right lower extremity sounds like a neurologic one. If the reflexes are hyperactive, an upper motor neuron lesion is apt to be present, possibly on a cerebrovascular basis; vascular lesions of the cord are known to occur. Finally, the patient may have a diabetic neuropathic condition in the peripheral nerves producing an areflexia at the knee or ankle. Certainly a neurologic examination is in order, for the paresis may be even independent of the generalized vascular sclerosis.

The advocate of intravenous ether therapy for diabetic gangrene, Dr. R. A. Katz, has abandoned the intramuscular use of ether because of the tissue reaction caused by the injection of ether into muscle. He later advocated the intravenous use of a 2.5 per cent solution of ether, 2 liters daily for twelve days, followed by a rest of two days after which twelve more daily treatments are given.

In a situation as described by the inquiry, the urge for active therapy should be tempered by the recognition of harm which may result from such treatment in a patient aged 88 years with a nerve lesion which is only indirectly vascular, perhaps purely diabetic.

CHILDREN'S SHOES

To the Editor:—**"Experts" in children's shoe departments have expressed widely divergent opinions on the type of shoe that should be worn by my children. Parents ask advice on the subject, and I have been unable to find a satisfactory answer. Assuming abnormality is absent and the proper size is worn, does it make any difference whether a child wears sandals, slippers, shoes with ankle support, soft or hard sole shoes, shoes with or without arch support, or shoes with or without an elevated heel? From the orthopedist's point of view, is there any contraindication for the normal child to go barefooted most of the time?**

M.D., Florida.

ANSWER.—The fourth line of the query contains an important assumption that might be debatable.

A child walks on the same surfaces as its mother and father; viz., hard floors, cement sidewalks and asphalt streets. It should have, therefore, the same degree of support and protection.

In the case of normal feet and a proper fit of shoes, it makes little difference whether the child wears sandals, slippers, shoes without ankle support, hard soles, shoes without arch supports or shoes without "elevated" heels (inquirer means "tilted" rather than "elevated" heels), providing occasional observation does not reveal ankle valgus or pronation.

Regarding the question of "going barefooted most of the time," the answer depends on the ground. The only places a child should go barefooted are in warm sand on a beach and in the bath tub.

SUBJECTIVE HEAT SENSATION

To the Editor:—A 35 year old Mexican male patient is robust, stout, apparently healthy and weighs 190 pounds (862 Kg.). He was in the Army for about four years, and served in Italy. On his discharge in 1945 all tests and examinations were negative in result. Two months ago he began experiencing a sensation of heat, or hot flash, which starts on the medial surface of the right foot about the plantar area and extends to the ankle. At times, it seems to involve the lateral surface of the right thigh. After the hot flash is over he says that it seems that the area involved contracts. This same sensation involves the nuchal area and the right side of the face, causing a similar feeling of contraction. Yet when he touches the areas involved they do not feel hot. His symptoms actually began in 1937, when for three days he had a hot sensation posteriorly beneath the lower rib margin. This feeling then extended to the neck, head and face with a tremor of the right lower eyelid. This was soon followed by generalized headache with nausea. On the third day of the attack, about 10 a. m. he lost consciousness, his head turned to the right, his face became cyanotic, and he salivated profusely. In about five minutes he "came to" and was taken to the emergency hospital, where he was released after a short period of rest. Diagnosis was not made and treatment was not given. He has consulted many physicians but has been unable to obtain relief from the feeling of heat in his foot, neck and right side of face. He has been told by various doctors that there is nothing the matter with him. The symptoms are aggravated when he gets angry or excited. Physical examination was essentially negative in result. The blood pressure was 130 systolic and 84 diastolic. Deep reflexes were hyperactive. Serologic reactions for syphilis are negative. He is nervous most of the time, stating that he is worried about having an attack, as in 1937. What suggestions do you have regarding diagnosis and treatment? He had the symptoms while in the Army but was told that he was shamming. M.D., Texas.

ANSWER.—In the absence of all objective evidence of involvement of the nervous system, the subjective complaints must be analyzed to decide whether it is likely that they reflect the presence of a disturbance in that system. One may encounter in nervous disorders, disturbances of long duration which, even though they disturb structure, may give no objective evidence that they exist. The subjective complaints must be analyzed with the following points in view: 1. Do they have a consistent anatomic distribution? 2. Do they have a consistent behavior, compatible with a disturbance of nerve function? In regard to the distribution, it is seen that the symptoms are always found on the right side of the body, involving the right foot and ankle, thigh, and the nuchal area and the right side of the face. This would correspond, if the condition is neurologic, to a disorder in the left hemisphere. However, there is no consistency as to the areas involved; it may be the foot or the thigh or the neck or the face. It is also pointed out that there is no progression of the symptoms over the body which would indicate "a cortical spread." If the subjective complaints were to start in the foot, they should then travel to the leg, the thigh, the trunk, then the arm and the face, and, if he is a right-handed man, some disturbance of language should be present.

The character of the symptom, which is a feeling of heat, could be of neurologic origin, but the fact that it is continuously present, especially in the foot, is a strong indication that it is not. Taken as a whole, the lack of consistency of the distribution of subjective complaints and the fact that the behavior of the complaints does not conform to that usually seen in organic disease of the nervous system would lead one to suppose that such does not exist. The nature of the disorder is not clear; the fact that it reproduces itself in somewhat identical fashion would lead one to believe that it is not an emotionally determined symptom; the possibility might be considered of a neurovascular disorder or even one of the disorders associated with histamine. While toxic phenomena are usually bilateral in character, it could be pointed out that histamine cephalalgia will usually occur only on one side of the face and repeat itself in identical fashion. It might be wise to give this patient a trial with antihistamine and/or ascorbic acid. One might determine whether histamine would precipitate or increase the subjective complaints.

IRRADIATED BLOOD

To the Editor:—What is the status of ultraviolet irradiation of the blood, and the "Knott hemo-irradiator"? Is it regarded as of clinical value?

Thomas P. Butcher, M.D., Emporia, Kan.

ANSWER.—There is no conclusive evidence that irradiation of the blood with ultraviolet light has merit. The studies in this field have suffered from the lack of adequate controls. The greatest possible usefulness of ultraviolet light in relation to blood lies in the radiation of pooled plasma to inactivate the virus of homologous serum hepatitis. However, the proper technic for such disinfection of plasma has not as yet been perfected.

EARLY ACQUIRED SYPHILIS

To the Editor:—A girl with active syphilitic lesions gave as her only source of contact a boy who had no history of either primary or secondary lesions and whose physical examination was normal. His qualitative Kahn reaction was positive. A quantitative test was not done at that time. He was treated with the twenty-six week Army plan of treatment consisting of forty injections of oxophenarsine hydrochloride and sixteen injections of bismuth compound. His blood Kahn reaction was still positive after treatment with eight quantitative units. Spinal fluid was normal. Three months later the blood Kahn reaction was doubtful. No therapy had been given. Please discuss further therapy of this case assuming that the blood Kahn reaction remains positive.

M.D., Kentucky.

ANSWER.—It seems likely that the boy had early acquired syphilis. The twenty-six week army plan of treatment is usually effective. The serologic response of the boy seems to be that of early syphilis adequately treated. At the end of treatment, the titer was 8 and three months later, it had dropped to doubtful. Ordinarily this indicates a satisfactory response, and a negative reaction should be expected within a few months. As some patients' serologic reactions decline in titer slowly, a period of eighteen months from the beginning of treatment should be permitted to elapse before further treatment is considered.

If at the end of eighteen months following the institution of treatment the reaction is still positive and no lesions are present, the boy may be considered to have seroresistant syphilis, or if the titer has risen, a serologic relapse, or a reinfection. In either event, the boy should be given the benefit of an adequate course of penicillin, for which there are many treatment schedules. A simple schedule is that of 600,000 units daily of penicillin-oil-wax for ten consecutive days. Subsequent to this, if the spinal fluid is again negative and the physical examination reveals no evidence of syphilis, no further treatment is indicated.

MALARIA

To the Editor:—Living in an area where malaria is epidemic, I am particularly interested in an editorial in The Journal (p. 1176, August 2, 1947) in which the idea was suggested that "plasmochin" is advocated for use in conjunction with pentaquine in the treatment of malaria due to Plasmodium vivax to eradicate extra erythrocytic forms. Is this now admitted as routine therapy? I understood that it was applicable only for malignant forms.

M.D., China.

ANSWER.—There is a misconstruction of the article which appeared in editorials and comments of THE JOURNAL wherein it was assumed that "plasmochin" was advocated in conjunction with pentaquine in the treatment of vivax malaria. The improved treatment of malaria with pentaquine includes its simultaneous use with quinine but not "plasmochin." Actually, pentaquine is a less toxic and more effective compound than "plasmochin" and replaces the latter in the treatment of malaria. The dosage used in studies to date is 2 Gm. of quinine and 30 mg. of pentaquine in three doses daily for two weeks. Although this therapy has not been used extensively in the field, it has been found that recurring cases among former servicemen have disappeared completely after this type of ambulatory treatment.

HYPOGONADISM

To the Editor:—Please outline the treatment of hypogonadism in a girl aged 22 who has no mammary development, no pubic hair, primary amenorrhea, no development of vagina and the frame of an immature girl.

Louis A. D'Alecy, M.D., Staten Island, N. Y.

ANSWER.—There is insufficient information to permit determination of whether this girl is suffering from primary pituitary insufficiency or from congenitally aplastic ovaries with sexual infantilism. The distinction is important, since treatment for the latter condition is so much more satisfactory. There are many physical signs which will help in the differential diagnosis, and there is one helpful laboratory procedure: assay of the urine for gonadotropins, which assay gives a high reading in the presence of aplastic ovaries and shows little or no gonadotropins in cases of pituitary insufficiency. Some encouraging results have been obtained with the use of estrogens in the treatment of girls suffering from congenitally aplastic ovaries. A recent review of this subject can be found in the October 1947 issue of the *Journal of Clinical Endocrinology* (Lisser, H.; Curtis, L. E.; Escamilla, R. F., and Goldberg, Minnie B.: The Syndrome of Congenitally Aplastic Ovaries with Sexual Infantilism, High Urinary Gonadotropins, Short Stature and Other Congenital Abnormalities. Tabular Presentation of Twenty-Five Previously Unpublished Cases, page 665).

HYPERTHYROIDISM AND PREGNANCY

To the Editor:—Please inform me regarding management of pregnancy with hyperthyroidism being adequately controlled with propylthiouracil. The patient is a young woman who had two previous pregnancies with a moderate nausea and vomiting in the first trimester. Thyroid enlargement and symptoms of toxicity developed about two years ago and reached a severe stage with extreme nervousness, weakness, weight loss, and tachycardia. Her basal metabolic rate was between plus 60 and plus 70. For the past five months symptoms have been absent and she has gained weight and strength. Tachycardia has disappeared, and her basal rate has dropped to the upper limits of normal. She receives 150 mg. of propylthiouracil daily. Two months ago she became pregnant; she is beginning to have anxiety symptoms, although there has been as yet no return to a toxic state.

Burrell F. Eckardt, M.D., Sheboygan, Wis.

ANSWER.—The literature dealing with hyperthyroidism in pregnancy was recently reviewed by R. O. Mussey, S. F. Haines and E. Ward (*Am. J. Obst. & Gynec.* **55**:609-618 [April] 1948). Thiouracil and related drugs have been used to control hyperthyroidism in pregnant women in a small number of cases reported in the literature. The occurrence of hyperplastic thyroids in a few of the fetuses calls for caution in the use of these drugs in pregnancy, although in a few cases they have been successfully used without demonstrable harmful effects. Of the goitrogenic drugs so far employed in the treatment of hyperthyroidism in pregnancy, reports seem to indicate that propylthiouracil can be used with greatest safety to the mother.

In 30 instances in which the patients received treatment at the Mayo Clinic, hyperthyroidism complicated pregnancy. The treatment carried out by Mussey, Haines and Ward included oral administration of Lugol's solution (strong iodine solution U. S. P.) and thyroidectomy for hyperfunctioning adenomatous goiters and Lugol's solution plus thyroidectomy, if needed, for exophthalmic goiter. Pregnancy did not seem to influence the course of hyperthyroidism in most cases. Likewise, proper treatment of the hyperthyroidism allowed the pregnancy to proceed normally. The standard treatment of hyperthyroidism by iodine and thyroidectomy can be carried out safely in the great majority of cases of hyperthyroidism complicating pregnancy and should be employed in this case if toxic symptoms appear.

HISTAMINE IN GASTRIC ANALYSIS

To the Editor:—References which I have for using histamine in gastric analyses say to use 0.1 mg. histamine for each 10 Kg. of body weight. Another reference advises 0.5 mg. as a total for the test in 1 cc. of solution. Does this quantity refer to histamine acid phosphate, or to histamine itself? If to the latter, may histamine acid phosphate be used in a gastric analysis? I have a solution of histamine acid phosphate, 0.55 mg. in 1 cc. (equivalent to histamine 0.2 mg.). In order to give 0.5 mg. histamine as my reference states, should I give 1 cc. of my present solution or give 2.5 cc. of the solution? In a recent patient whose blood picture was that of pernicious anemia I found no free hydrochloric acid after alcohol or histamine. The amount of histamine used was 0.55 mg. histamine acid phosphate. The patient weighed 150 pounds (68 Kg.). Is this a satisfactory test?

M.D., Kentucky.

ANSWER.—On looking over the statements regarding this subject in standard reference books, one is amazed at the differences in dosages suggested. Some of this confusion apparently arises because of the number of preparations of histamine which are commercially available. The drug may be purchased as acid phosphate or the dihydrochloride. The active portion of these substances is the histamine which they contain. The amount of histamine base in acid phosphate represents 36 per cent and in the dihydrochloride 60 per cent. The dosage used should always be calculated in terms of the histamine base. Either salt may be used, and both of the compounds should be dissolved in isotonic sodium chloride solution.

The usual dose of 0.1 mg. of histamine base for each 10 kilograms of body weight may perhaps be a little high. No harm will be done, however, if no more than 0.7 mg. is used. Satisfactory results can be obtained by using 0.3 to 0.5 mg. of histamine base.

ACNE VULGARIS

To the Editor:—I am seeking information on the treatment of acne vulgaris with estrogenic substances, particularly in male patients. What are specific dosages, therapeutic regimen and limitations of this therapy?

Lieut. Donald H. Ewalt, M.C., Fort Sill, Okla.

ANSWER.—Estrogenic substances should not be used in the treatment of acne in either boys or girls. They may have a profound effect on the patient, which would not be desirable. There is no assurance that they would have a good effect on the acne itself. It is suggested that other methods be employed for acne rather than hormone therapy.

ANAL FISTULA

To the Editor:—Kindly inform me whether there is any treatment for anal fistula and perianal abscesses except surgical treatment.

Oscar Gelbart, M.D., Ossining, N. Y.

ANSWER.—In every kind of anal fistula and abscess, there is an opening into the bowel with a tract leading through the soft parts to the skin. In order to obtain a cure, this opening in the bowel must be closed. Small tracts have closed as a result of inflammation. Such small openings may possibly heal spontaneously if the patient is given succinylsulfathiazole or sulfaguanidine, 3 or 2 Gm. four times a day, and, in addition, if he takes a 10 ounce water enema every day before movements.

Some surgeons have tried treatment by injection of sclerosing solutions such as sodium morrhuate. If this is done when infection is present the bacteria that are present in the bowel are apt to produce an abscess. The result is uncertain and the results with surgery properly executed are so satisfactory that there is little reason to attempt treatment by injection.

AMMONIATED MERCURY

To the Editor:—In the treatment of dermatitis of the scalp is it safe to apply a 5 per cent ammoniated mercury ointment to the entire scalp? Could such an ointment give rise to a toxic reaction? Does any pharmaceutical house supply ammoniated mercury in a water-miscible base?

M.D., Florida.

ANSWER.—Dermatologists not infrequently prescribe ammoniated mercury in 5 per cent concentration for use on the entire scalp in adults. Ordinarily the concentration is reduced for use in children. Unless the patient is sensitized to mercury, there would be no reason to expect trouble from its use, for usually the ointment is applied only for short periods and little of it is required to cover the scalp. The ointments containing mercury which are prepared by pharmaceutical houses for the market apparently are not made with water-miscible bases.

RESIN DERMATITIS

To the Editor:—Please discuss methods of prevention of contact dermatitis from a resin used in gluing plywood together called "P. R. 14" or "amberlite" made by the Resinous Products and Chemical Company, Washington Square, Philadelphia 5.

M.D., Wisconsin.

ANSWER.—In order to prevent dermatitis from resin, it is necessary to avoid contact with it, for desensitization to resin cannot be induced. If it is impractical to wear gloves during work, contact can be avoided by wearing any of the so-called chemical or invisible gloves or protective ointments that are advertised for use in industry. There are several available on the market. They serve adequately to protect the skin against the action of irritants except when it is necessary to wet the skin, for these protective preparations are usually soluble in water.

PAGET'S DISEASE

To the Editor:—Please give information on the use of aluminum acetate in the treatment of Paget's disease.

Samuel Waldman, M.D., Brooklyn.

ANSWER.—Agreement is lacking amongst authorities as to whether aluminum acetate in the treatment of Paget's disease does any real good. However, one is dealing with a chronic disease and there is sufficient evidence from reliable observers to warrant at least a trial of the drug in treating Paget's disease (Paget's bone disease or osteitis deformans).

The aluminum acetate solution is made in the following proportion:

Solution aluminum acetate (Burow's solution)	8 ounces
Syrup of tolu	3 ounces
Honey sufficient to make	16 ounces

1 teaspoonful two or three times daily

HERPETIC STOMATITIS

To the Editor:—I should like to supplement the answer to the query on "herpetic stomatitis" in The Journal, Dec. 13, 1947, page 1040. First, herpetic stomatitis is not necessarily accompanied by external lesions of herpes simplex, as the writer states; such an association is exceptional. Second, it is by far the most frequent reason for recurrent oral ulceration over a period of many years. Finally, it is almost always relieved, and sometimes actually cured, by repeated vaccination against smallpox or, perhaps better, repeated biweekly intradermal injections of smallpox vaccine suspended in saline solution. The technic is described in detail in the *Proceedings of the Staff Meetings of the Clinic, Honolulu*, for August 1944.

Harry L. Arnold Jr., M.D., Hawaii.